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# ANNALS OF THE RHEUMATIC DISEASES

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# IDIOPATHIC EXTREME OSTEOPOROSIS, ESPECIALLY OF THE SPINAL COLUMN AND THORACIC CAGE, WITH COLLAPSE OF FRONT OF CHEST

BY

H. C. LAUBER, F. PARKES WEBER, and J. G. GREENFIELD

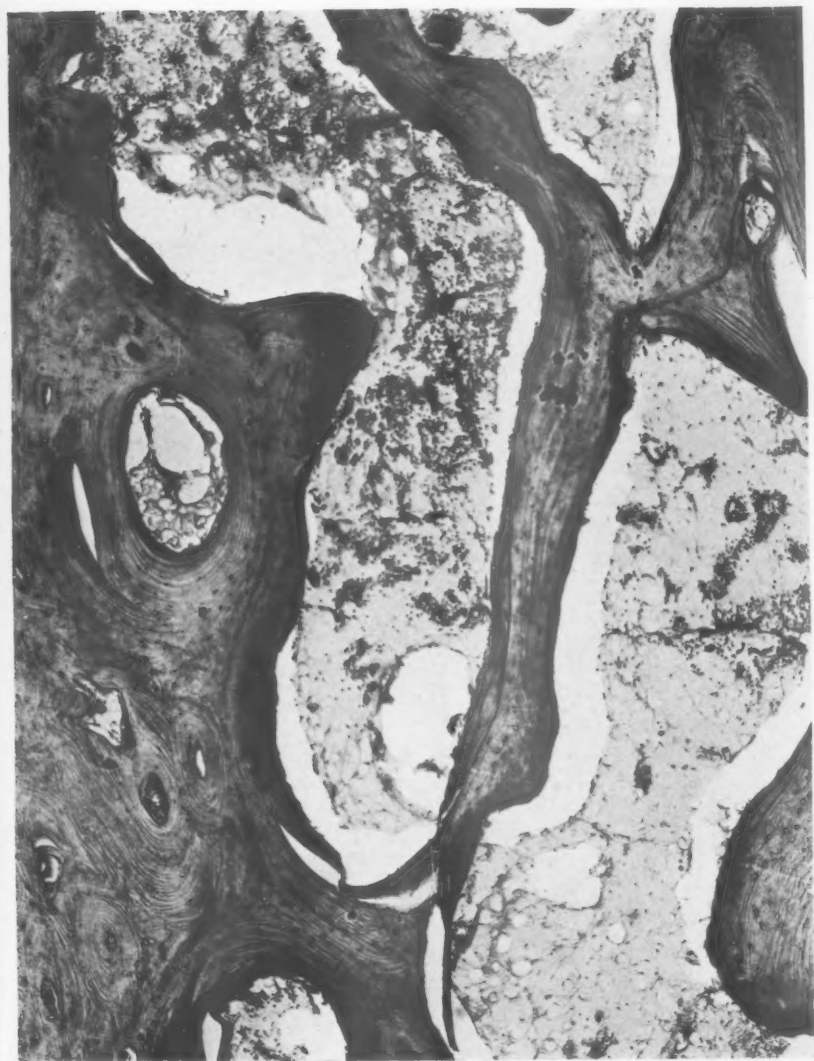


FIG. 1.—Section of skull showing rather thinned trabeculae of bone in diploe and partial disappearance of marrow cells.  $\times 55$ .

By "idiopathic" we mean of unknown causation. Burrows and Graham (1945 and 1947) describe a condition of spinal osteoporosis of unknown causation due to deficient ossification, affecting adults above 30 years of age, mainly women of 55 to 80, but also men, commonly between 40 and 70. Though the cause is unknown, it is suggested that it may possibly be related to slight dietary deficiency of calcium, phosphates, and ascorbic acid, but it is not due to deficiency of vitamin D. With calcium medication, they say, the symptoms improve, but there is little or no demonstrable improvement in regard to the osteoporosis.

They write: "Although generalized osteoporosis can sometimes be demonstrated, a *material degree of porosis* is confined to those bones, which, in the adult, contain red bone-marrow, namely, those of the spine, limb girdles, and thoracic cage. Only the lumbar and thoracic vertebrae undergo sufficient porosis to suffer *material deformity*." Our present case differed from all the severe ones to which Burrows and Graham (1947) refer, inasmuch as the actual bony collapse was relatively slight in the vertebral column, but so extreme in the



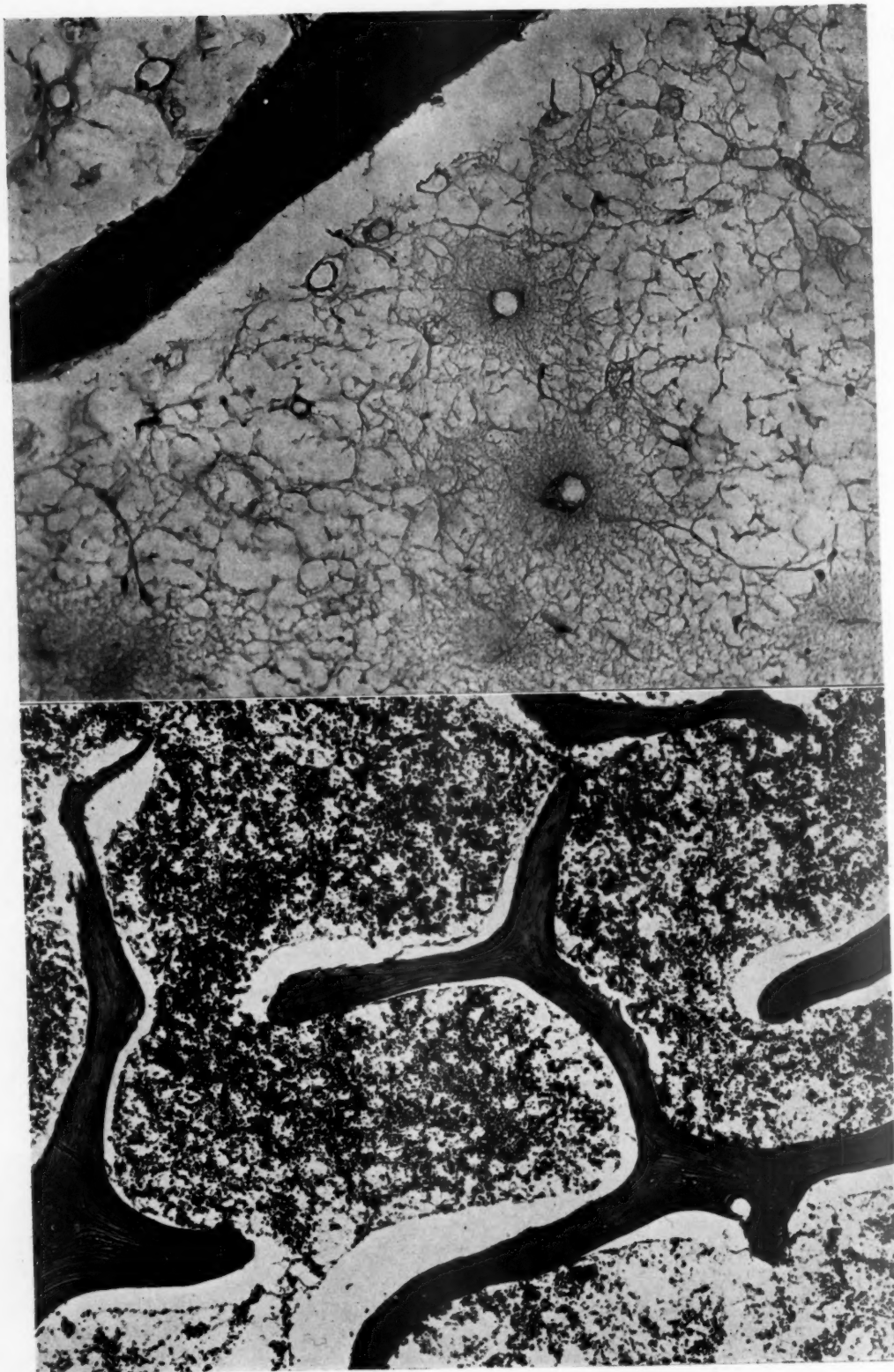


FIG. 2.—Section of vertebral body showing very thin bony trabeculae. In this area the loss of marrow cells is only slight.  $\times 55$ .

FIG. 3.—Section of vertebral body, an area from which the marrow cells have disappeared completely leaving a thin areolar tissue.  $\times 180$ .



thoracic cage as to cause collapse of the front wall and falling in of the sternum.

#### Account of the Case

The patient, a manufacturer, aged 44 years, was admitted to hospital under Dr. H. C. Lauber on Nov. 12, 1943.

**HISTORY.**—The family history was not relevant. There were no brothers or sisters. In 1923: "chronic cholecystitis with hypochlorhydria" had been diagnosed (dislike of fatty food, blown-up feeling, flatulence). Since 1930 he had suffered on and off from "fibrositis". In 1937 a tumour of the brain was diagnosed by Dr. H. Cohn and operated on by Sir Hugh Cairns. An oligodendroglioma was removed. After that the patient felt well, except that in 1940 he suffered from sinusitis.

Since January, 1943, he had from time to time noticed pain in his back, for which he had massage. The pain gradually got more severe, and in October he noticed that he could lie in a certain position only and that the pain was most pronounced on getting up in the morning. At the beginning of November, 1943, the pain was especially felt in his right side, and he went to hospital with the suspicion of having pleurisy.

**CONDITION IN HOSPITAL.**—He was a thin, pale-looking man without dyspnoea and without cyanosis. Cardiovascular system, chest organs, abdomen, and central nervous system were normal. The dorsal and lumbar spine was stiff, and most painful when bending down or sideways. The joints of arms and legs were normal, and so was the temperature. Cholecystography showed that the gall-bladder did not fill. The Wassermann reaction was negative. The erythrocyte sedimentation rate was 28 mm. (2 hours' average). The urine contained a trace of albumin, no sugar, a few hyaline casts, and no Bence-Jones protein.

The blood count was: haemoglobin 70 per cent.; erythrocytes 3,760,000 per c.mm.; colour index, 0.93; leucocytes 9,600 per c.mm. The blood calcium was 9.5 mg. per 100 c.cm.

Radiographic examination of the spine was performed by Dr. Roth, who found partial collapse of the tenth dorsal vertebra and osteoporosis of the vertebral column. The skull showed marks of the previous operation.

In December, 1943, the patient had a spell of partial mental disorientation and drowsiness lasting for two weeks. On Dec. 6 the urine showed no trace of albumin or sugar; the blood-urea was 122 mg. per 100 c.cm. On Dec. 15 there was a trace of albumin in the urine, and also a few hyaline and granular casts. The blood urea was 137 mg. per 100 c.cm.

Urological examination (Dr. Dannheisser) did not show signs of obstructive uraemia. Fluid intake was 55 oz., and fluid output 48 oz.

At the end of December the blood urea was 103.6 mg. per 100 c.cm.

By January, 1944, the patient recovered from this uraemic condition. He complained of increasing pain in the back and chest on and off. His anaemia increased; his strength deteriorated, though his appetite was very good. On Jan. 15 the blood count was: haemoglobin 40 per cent.; erythrocytes 1,980,000 per c.mm. of blood;

colour index 1.02; leucocytes 7,800 per c.mm. The differential count (per cent.) was: neutrophils 36, neutrophils stab. 8, neutrophils juv. 1, lymphocytes 51, monocytes 2, eosinophils 2 (macrocytosis, hyperchromia, aniso-poikilocytosis).

In the same month the urine was acid with a specific gravity of 1012; there was a trace of albumin, but no Bence-Jones protein. Microscopic examination revealed hyaline and cellular casts and leucocytes.

On Feb. 12 the blood count was: haemoglobin 42 per cent.; erythrocytes 2,160,000 per c.mm. of blood; colour index 0.98; leucocytes 6,900 per c.mm. Total protein in the blood: 6.2 per cent.

By March, 1944, his condition had not altered much; there was further loss of flesh in spite of a diet high in calories. On Mar. 15 the blood count was: haemoglobin 52 per cent.; leucocytes 6,100 per c.mm. of blood. The differential count (per cent.) was: neutrophils 47, neutrophils stab. 2, neutrophils juv. 1, lymphocytes 47, monocytes 3.

The leucocytes showed toxic granulation, and the erythrocytes hypochromia with anisocytosis. The blood urea was 65.4 mg. per c.cm.

Radiographs were taken of the thorax, spine, pelvis, and femur: all bones were shell-like and showed advanced changes. There was spontaneous fracture of one rib, and gross changes were noted in the skeleton of the chest wall.

Repeated examination showed a trace of albumin in the urine, but no Bence-Jones protein.

On May 25, 1944, the blood count was: haemoglobin 46 per cent.; erythrocytes 2,680,000 per c.mm. of blood; colour index 0.80; leucocytes 7,100 per c.mm. The differential count (per cent.) was: neutrophils 57, lymphocytes 40, monocytes 1, basophils 2. There was toxic granulation and aniso-poikilocytosis.

Unfortunately the blood which was taken for estimation of phosphatase and phosphorus was lost on two occasions, and these important data are therefore missing.

On Aug. 28, 1944, the blood count was: haemoglobin 54 per cent.; erythrocytes 3,240,000 per c.mm. of blood; colour index 0.80; leucocytes 7,300 per c.mm. The differential count (per cent.) was: neutrophils 40, lymphocytes 56, promyelocytes 3, plasma cells 1.

There was fracture of another rib, and the patient was feeling weaker and was much thinner. There was temporary corneal erosion, much pain when moving, and "falling in" of the sternum. He died on Sept. 13, 1944.

**TREATMENT.**—Between Nov. 12, 1943, and Jan. 19, 1944, he had "fersolate"; vitamin D (calciferol), and injections of colloidal calcium. In January, 1944, a leather jacket was given to him, but it was never worn. From May 25, 1944, radiostoleum and calcium were given by mouth. Beginning on June 18 he received twenty injections of colloidal calcium, after which, from July 20, he had twenty injections of calcium (Sandoz).

On Aug. 25, 1944, morphine was started.

**NECROPSY.**—There was extreme emaciation. The organs were pale and very reduced in size and weight; the bones of the thoracic cage and vertebral bodies were shell-like, and there was osteoporosis of all bones,

especially of the spine. The bone-marrow of one of the iliac bones was examined and found macroscopically to resemble that of the ribs. The bone-marrow was partly gelatinous. The macroscopic appearance of the internal organs was normal except for their small size. The weight of some of the organs was as follows:

		Normal average
Brain .. ..	1,250 g.	1,358 g.
Heart .. ..	200 g.	300 g.
Liver .. ..	700 g.	1,600 g.
Spleen .. ..	250 g.	250 g.
Kidney (left) ..	150 g.	150 g.

The following were sent for pathological examination to Dr. J. G. Greenfield, at the Chase Farm Hospital, Enfield: pieces of spleen, liver, and aorta; the urinary bladder with the prostate gland, the thyroid gland, a suprarenal gland, and the pituitary gland; the left kidney and brain; the greater part of the vertebral column with ribs attached; part of the right ileum; the central part of the right femur (with gelatinous bone-marrow), the sternum, with the whole front of the chest; and the calvarium. Unfortunately the pituitary gland was lost.

#### DR. GREENFIELD'S HISTOLOGICAL (AMENDED) REPORT

**Spleen.**—In the spleen there was thickening both of the fibrous tissue septa and of the adventitia of the blood vessels. No Malpighian bodies were seen. The arterioles were thick-walled but without hyaline change in the media. There was diffuse fibrosis of the pulp, and a very large amount of blood pigment collected in masses or in smaller intracellular collections. There was a diffuse increase in the numbers of lymphocytes and plasma cells in the sinus system.

**Liver.**—The liver cells also contained a large amount of blood pigment, most of which gave the Prussian Blue reaction; swollen Kupffer cells were also seen full of Prussian blue granules. There was also some excess of bile pigment in the liver cells. There was no excess of lymphocytes in the portal tracts.

**Aorta.**—The aorta was normal. The thyroid showed diffuse fibrosis but no evidence of hyperactivity.

**Kidney.**—In the kidney there was a diffuse deposition of small calcified knots in the interstitial fibrous tissue, both in the cortex and medulla. Some small wedges of degeneration and fibrosis were seen passing in from the capsule. The smaller arteries showed slight concentric and eccentric thickening of their walls, but no hyaline degeneration of the media. Some of the glomeruli showed slight hyaline changes.

**Brain.**—In the area of the brain from which the tumour had been removed there was softening of the subcortical white matter over a limited area, with collagenous and neuroglial scarring, calcium deposition in this and the zone immediately surrounding it, and the presence of many granular and other phagocytic cells.

**Prostate.**—The prostate showed an excess of small calculi (prostatic sand) but no other abnormality.

**Bones.**—In the dark areas the skull contained fairly large Haversian canals which were filled chiefly with thin areolar tissue, but many contained also rather sparse

marrow cells ("Gelatinous degeneration of bone-marrow"). There was some irregularity in the lines of ossification, but no evidence of osteoid tissue. The vertebral bodies showed extreme osteoporosis, only a very thin outer shell of bone remaining, with some thin spicules of bone in the medulla. Here the marrow cells were in places very sparse and in places absent. In the latter areas the connective tissue was of finer character than in the skull.

#### Discussion

Extreme spinal and thoracic osteoporosis, with resulting deformity, may, as Burrows and Graham (1947) point out, be found in known diseases causing osteoporosis, and similar deformities may, as is well known, occur in osteomalacia. One of us (Parkes Weber, 1897), under the heading "general lymphadenosis of bones, one form of multiple myeloma", described the case of a man, aged 61 years, whose spinal column and thoracic cage were infiltrated and largely replaced by some kind of a malignant very vascular neoplasm. The bones and microscopic sections were carefully examined by the late Prof. S. G. Shattock, by whom specimens were arranged and described in the museum of the Royal College of Surgeons in London (catalogue, 2115 D, 1640 E, 1640 F). No similar case has been met with since then. The ribs were all converted into delicate tubes formed of periosteum with only a thin imperfect shell of bone; they were stuffed full of the new growth.

In regard to the collapse of the front wall of the thoracic cage and the consequent falling in of the sternum, one of us (Parkes Weber) has seen a similar appearance in a young man, but that was the case fully described by Graham and Stansfeld (1946) under the heading "A Hitherto Undescribed Lipoidosis simulating Rheumatoid Arthritis".

Whether cases similar to those described under the heading "Milkman's disease" are in any way related to idiopathic spinal osteoporosis seems to be answered in the negative by McCance's paper (1947) on "Osteomalacia with Looser's nodes (Milkman's Syndrome)" due to abnormal resistance to absorption of vitamin D. The term Looser's zones is probably preferable to Looser's nodes.

A question which arises, and cannot yet be answered, is whether cases of severe or less severe idiopathic spinal osteoporosis are related in any way to the ordinary cases of generalized osteoporosis in old age (Kesson and others, 1947). (See also Black and others, 1941, and Merklen, 1936.)

As to the cause of the haemolytic anaemia in the present case, it seems highly probable that it was in some way connected with, if not directly due to, the changes in the bone-marrow.

It is unfortunate that owing to wartime difficulties

our data are incomplete with regard to the blood phosphorus, the blood phosphatase, and histological examination of the pituitary and parathyroid glands. However, it is unlikely that the temporary renal disturbance, evidenced especially by high blood urea, caused secondary hyperparathyroidism; no excess of blood calcium was discovered.

#### Summary

The case was that of a man, aged 44 years, who in January, 1943, commenced to suffer on and off from pain in the back. Signs of severe osteoporosis of the vertebral column and ribs gradually increased, and were accompanied by considerable anaemia. He died in September, 1944. The necropsy showed osteoporosis, especially of the vertebral column and chest wall. As in similar (though somewhat less extreme) cases recorded in the literature of the subject, no cause was discovered, and all treatment was unavailing. The actual bony collapse was less in the vertebral column than in the thoracic cage, where falling-in of the sternum was a result.

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#### Ostéoporose Idiopathique Grave, Atteignant Particulièrement la Colonne Vertébrale et la Cage Thoracique avec Effondrement Frontal du Thorax

#### RÉSUMÉ

Le malade était un homme, âgé de 44 ans, qui avait commencé, en janvier 1943, à souffrir de douleurs intermittentes dans le dos. Les symptômes d'ostéoporose grave de la colonne vertébrale et des côtes, accompagnée d'anémie très prononcée augmentèrent graduellement. Il est mort en septembre 1944. A l'autopsie on constata de l'ostéoporose, surtout de la colonne vertébrale et des parois thoraciques. De même que dans les cas analogues cités dans la littérature, on n'a pu en déceler la cause, et aucun traitement n'a donné de résultat. L'affaïssement osseux était moins marqué dans la colonne vertébrale que dans la cage thoracique où il avait provoqué le renforcement du sternum.



# MUSCLE HISTOLOGY IN RHEUMATIC AND CONTROL CASES: A STUDY OF ONE HUNDRED AND NINETEEN BIOPSY SPECIMENS

BY

M. H. L. DESMARAIS, H. J. GIBSON, and G. D. KERSLEY

*From the Royal National Hospital for Rheumatic Diseases, Bath*

## Introduction

Our conception of the pathology of rheumatoid arthritis has become modified as the result of recent studies of the widespread changes taking place in the non-articular tissues in this disease. Gibson and others (1946) confirmed the work of Freund and others (1945) by showing that the affected tissues were all of mesodermal origin and that the lesions found in muscles consisted of a perivascular round-cell reaction in the endomysium and of a paravascular cell reaction in the fibrous supporting connective tissue. The blood vessels were sclerosed, with proliferation involving all three coats, and a cell infiltration, almost entirely lymphocytic in type, appeared to originate in the adventitia and to spread outwards. The individual muscle fibres showed evidence of degeneration. This range in degree from loss of striation, longitudinal fissuring, and vacuolation, to the formation of scar tissue enclosing degenerated shrunken muscle fibres. Muscle-fibre degeneration was frequently more marked near the cellular infiltrations.

It was suggested that the relationship of the reaction to the blood vessels might indicate that the noxious agent was a blood-borne irritant, but there was no evidence to show whether or not it was infective in origin. de Forest and others (1947) reported the presence of muscle lesions in twelve out of sixteen cases of rheumatoid arthritis, and in two of four controls of "non-specific infectious" arthritis. They could find no relation between the presence of the lesions and the duration or activity of the disease. Thirteen other controls, consisting of cases of osteo-arthritis, rheumatic fever, gonococcal arthritis, and "non-specific infectious arthritis" failed to show the muscle lesions as seen in rheumatoid arthritis.

Since our previous communications (Gibson and others, 1946; Kersley and others, 1946) further examinations of material obtained either by biopsy or at operation have been carried out on a series of fifty-six typical cases of idiopathic rheumatoid arthritis, five of non-specific infective arthritis, forty-three other rheumatic conditions, and fifteen non-rheumatic controls.

## Methods

The biopsies were taken under local anaesthesia either from the deltoid or the quadriceps muscles, and in two cases from the erector spinae muscle. The material collected at operation was excised from the vastus externus in cases of arthrotomy and knee lavage, and from the vastus internus when a synovectomy was performed. The muscle excised did not always show evidence of wasting clinically, and the neighbouring joints were not necessarily affected.

The amount of muscle taken was sufficient to give a stained section of approximately 13 mm. by 8 mm. on the average, although the actual size varied considerably with the circumstances of its removal. Portions removed at operation under general anaesthesia were larger than those taken under local anaesthesia.

Many fixatives were used including Zenker, formol sublimate, and 5 per cent. formol saline. Zenker was best, but the results with 5 per cent. formol saline were quite satisfactory. The tissue was then passed through industrial spirit, acetone, and benzene, and embedded in the vacuum bath. The routine stain was iron haematoxylin and eosin. Other stains used in certain cases were Masson's trichrome, Foot's reticulin stain, and Unna-Pappenheim stain for plasma cells.

In order to obtain an unbiased assessment of the experimental findings the cases were carefully examined clinically and grouped according to a tentative classification. The biopsy material was reported on by the pathologist without knowledge of the clinical findings. The pathological and clinical data were later correlated.

The sedimentation rate and haematocrit were estimated by the method of Collins and others (1940). The corrected suspension stability (C.S.S.) is the percentage volume of red cells after one hour corrected for any anaemia present, taking a haematocrit reading of 42 per cent as being normal. A corrected suspension stability of 85 per cent. or more is taken as normal, and a reading below 60 per cent. is considered maximal.

### Classification and Definition

Cases of non-specific polyarthritis were divided into two groups:

1. Typical idiopathic rheumatoid arthritis;
2. Non-specific infective arthritis.

The idiopathic type is liable to affect the young adult or middle-aged individual. It is five times more common in women than in men and usually occurs between the ages of 15 and 45. It is characterized by general constitutional and autonomic disturbances, accompanied sometimes by a low fever. There is early muscle wasting, the sedimentation rate is raised, and anaemia is present. Generalized osteoporosis is an early sign. The polyarthritis tends to effect symmetrically the smaller peripheral joints first, and to spread to the other joints later. If untreated it ends in contractures, subluxations, and ankyloses.

In the non-specific infective type the occurrence in men is less rare. The age incidence has a wider range. The onset is sometimes acute and often follows an infection in the sinuses or the throat, an apical abscess, or a pelvic condition. The larger joints tend to be affected earlier than the smaller and the joint involvement is less symmetrical. The sedimentation rate has a tendency to fluctuate, and there may be little loss of weight. If a focus of infection is found and dealt with, the prognosis is usually good. The osteoporosis is not generalized but is more evident at the site of the involved joints. It must be remembered, however, that there exist all gradations between the two types, and especially in the later stages differentiation may be very difficult. Whenever there was doubt the case was included in the idiopathic rheumatoid arthritis group.

### TYPICAL IDIOPATHIC RHEUMATOID ARTHRITIS

Of fifty-six cases of typical idiopathic rheumatoid arthritis investigated, 34 (60.7 per cent.) showed round-cell foci and blood-vessel changes. Twenty-two out of thirty-eight men of ages varying from 15 to 65 years, and twelve out of eighteen women of ages varying from 35 to 56 years were positive. The bigger number of males in this series was due to the fact that it was easier to obtain their consent

to have a biopsy done. The size of the sections varied between  $6 \times 8$  and  $20 \times 10$  millimetres, the average being  $13 \times 8$  millimetres wide. The fact that the lesions were found in such small specimens in as high a proportion as 60.7 per cent. is an indication of their widespread distribution.

In one case two small foci were seen on the very edge of the section, and when further serial sections were made from the same block at a different level no other foci could be demonstrated. Had the muscle specimen been slightly smaller or been taken from a different site the histo-pathological changes found might have been absent and a negative report would have been sent by the pathologist. This indicates the importance of the sampling error in assessing results.

Several cases which were clinically and radiologically typical of idiopathic rheumatoid arthritis with varying degrees of muscle wasting showed histologically marked degenerative changes in the muscle fibres but the typical round-cell foci were not present. These cases were included in the negative group.

**Relationship of Positive Findings to Activity.**—The changes in the muscles were present not only in cases in which the disease was active but also in those which appeared clinically quiescent or "burnt out", as judged by the absence of resting pain and anaemia, constant weight or gain in weight, and

TABLE 1  
RELATIONSHIP OF FINDINGS TO ACTIVITY

Findings	Number of cases	No anaemia	Normal C.S.S.	No anaemia and normal C.S.S.
Positive	34	11 (32.3%)	5 (14.7%)	3 (8.8%)
Negative	22	10 (45.4%)	4 (18.1%)	3 (13.6%)

normal sedimentation rate. Table 1 shows the number of negative and positive biopsies in such cases. Two cases could be quoted: One showed marked muscle wasting and the other no wasting of the muscle from which the biopsy was taken, but both were of long standing and apparently "burnt out". Each showed the round-cell foci as seen in rheumatoid arthritis.

CASE 77.—A farm worker, aged 41, gave a history of rheumatoid arthritis of 15 years' duration. All the joints except the hips and spine and to a very slight extent the knees, were involved. The quadriceps from which the biopsy was taken showed no clinical evidence of wasting. There was no anaemia, and the sedimentation rate was normal. There were no joint pains. He



had had several courses of gold with fairly good results. The weight had remained constant for many years. Radiographs of the hands showed changes of rheumatoid type, with secondary osteo-arthritis. The muscle biopsy was taken from the right vastus externus and a section showed the typical changes consistent with rheumatoid arthritis (Fig. 1).

**CASE 10.**—A housewife, aged 56, had typical rheumatoid arthritis of 24 years' duration with marked muscle wasting. She had had two courses of gold with good results. Recently she had much improved and was gaining weight and had no pain in her joints even on movement. There was no anaemia, and the sedimentation rate was normal. Radiographs of the hands showed changes of rheumatoid type with secondary osteo-arthritis. The muscle biopsy was taken from the left vastus externus, and on section again several round-cell foci were seen.

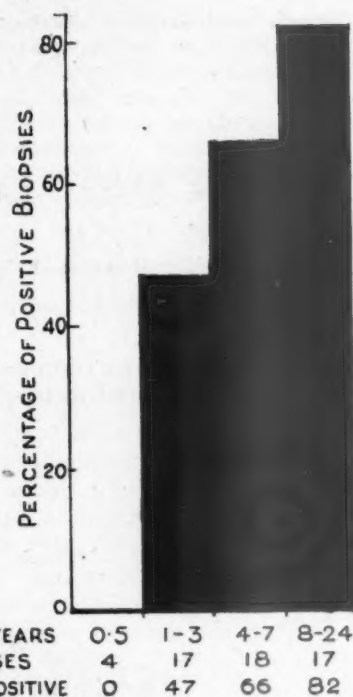
**Relationship to Wasting.**—The lesions were not found only in cases in which muscle wasting was present. Two cases, with good muscular power, full range of movements of the hip and knee joints, and no clinical evidence of wasting of the quadriceps, showed changes consistent with rheumatoid arthritis. One had typical rheumatoid arthritis of 15 years' duration which had become relatively quiescent as judged by the absence of anaemia, lack of joint pains, and x-ray evidence of superadded secondary osteo-arthritic changes in the joints of the hands.

The other was of 4 years' duration and was still active at the time of the biopsy.

**Relation to duration.**—An attempt was made to correlate the frequency of positive findings with the duration of the disease. The accompanying graph shows that no typical rheumatoid changes were found in cases of less than 6 months' duration. In those examined within three years, seven years, and from 8 years onwards the chances were 47 per cent., 66 per cent., and 82 per cent. respectively. The lesions were present in cases of from one to 24 years' duration.

**Relation to other Morbid Histological Findings.**—In two cases muscle biopsies were negative, yet there were other positive morbid histological findings. The first case showed no lesions in the muscle, but two subcutaneous nodules excised from the elbows were typical of rheumatoid arthritis. In the second case the muscle specimen was also negative but the synovia showed Allison and Ghormley round-cell foci.

**CASE 100.**—A housewife, aged 31, had typical rheumatoid arthritis of 7 years' duration. Her knees had never troubled her much and the quadriceps were not wasted. Her weight had remained constant but she was anaemic and the sedimentation rate was raised (C.S.S. 71 per cent.). The muscle biopsy from the vastus externus showed no round-cell foci and very little muscle degeneration,



GRAPH showing relationship between duration of disease in years and percentage of positive biopsies.

tion, but two large subcutaneous nodules excised from the elbows showed the changes typical of rheumatoid arthritis.

**CASE 83.**—An ex-miner, aged 57, had been suffering from rheumatoid arthritis for two years, during which time he had lost nearly 2 stone in weight. There was no anaemia (haematocrit 42 per cent.) but the sedimentation rate was raised (C.S.S. 60 per cent.). The plasma uric acid was 5 mg. per cent., and the Kahn test was negative. The x-ray appearances of the hands were of the rheumatoid arthritic type. Muscle and synovial material collected at operation for bilateral knee lavage were both negative. The synovia showed a non-specific chronic inflammatory reaction with diffuse round-cell infiltration but no foci of the Allison and Ghormley type. When a synovectomy on the right knee was performed 5 months later the synovia showed an extremely active round-cell reaction with, in certain of the villi, localized lymphocytic accumulations as seen in rheumatoid arthritis.

The findings in this last case are of interest in view of the report by McEwen and others (1941). Using the supravital method of staining they examined synovial tissue from cases of tuberculous and rheumatoid arthritis and also from cases with traumatic joint disturbances and synovitis of unknown cause and from two cases of poliomyelitis. In all these cases small and medium size fixed tissue cells were demonstrated. Bennett



(1941) studied 155 cases of arthritis and showed that a chronic inflammatory reaction, which frequently contained no diagnostic features, could be demonstrated in the synovia, and he came to the conclusion that the finding of lymphoid accumulations with or without germinal cells was not specific for rheumatoid arthritis.

Seventeen of the thirty-four typical rheumatoid arthritic patients with positive muscle findings showed other positive histo-pathological changes also.

TABLE 2  
RELATIONSHIP OF POSITIVE AND NEGATIVE MUSCLES TO OTHER MORBID HISTOLOGY FINDINGS

Number of cases	Diagnosis	Muscle	Synovia	Nodule	Skin
1	Rheumatoid arthritis	+	0	+	0
1	"	+	+	+	0
2	"	+	0	0	—
13	"	+	+	0	0
3	"	—	0	+	—
1	"	—	+	0	0
1	Still's	—	0	0	+

0=not examined.

Table 2 illustrates these findings. In some cases biopsies from two different sites were taken. In one the deltoid showed no changes but the quadriceps gave a positive result, and in the other both the quadriceps and the deltoid muscles showed the presence of round-cell foci.

Curtis and Pollard (1940) were the first to describe small perivascular infiltrations with lymphocytes in the corium of the skin in cases of rheumatoid arthritis and Felty's syndrome. In two cases with positive and three with negative muscle findings, the skin appeared normal. However, in a case of Still's disease (Case 72) though the underlying muscle appeared normal there were several areas of perivascular round-cell infiltration in the corium. The cells were lymphocytes and in each focus as seen in the stained section fifty or more were seen in the interstices of a fine network of collagen fibrils. In one instance such a focus was adjacent to a bundle of arrectores pilorum muscles. It appeared to be eroding the muscles, displacing and breaking up the fibres, fragments of which could be seen within the focus in Masson-stained sections (Fig. 2).

**Rheumatoid Arthritis with a Past History of Rheumatic Fever.**—Four cases of rheumatoid arthritis gave a history of previous attacks of rheu-

matic fever, one of which showed typical round-cell foci, and another evidence of an early focus in the muscle examined.

CASE 71.—A woman, aged 46, had had two attacks of rheumatic fever at the ages of 10 and 21. The heart was not involved. At the age of 30 she had had a third attack, which was soon followed by permanent joint changes, flexion deformity, and stiffening of the fingers wrists, elbows, and knees. There was marked muscle wasting. Previous to admission she had had an attack of herpes zoster of the right leg accompanied by an exacerbation of the joint pains. The haematocrit was 33 per cent. and the sedimentation rate raised (C.S.S. 67 per cent.). The x-ray appearances of the hands were typical of rheumatoid arthritis with secondary osteo-arthritis changes. The histological appearances of the muscle are figured in our earlier paper (Gibson, Kersley and Desmarais, 1946, Fig. 3).

CASE 42.—A woman, aged 32, gave a history of three attacks of rheumatic fever at the ages of 14, 22, and 25. The heart was again normal. Soon after the third attack she developed the typical changes of rheumatoid arthritis. There was marked muscle wasting with moderate deformity. She had had fourteen courses of gold but developed toxic symptoms with the last. The haematocrit was 35 per cent. and the sedimentation rate was normal (C.S.S. 89 per cent.). It is interesting to note that this patient too, had had an attack of "shingles" at the age of 22. A muscle biopsy was done on the left deltoid and the section showed histological evidence of early foci. The muscle showed very slight degenerative changes and no arterial disease was seen. Two very small foci were found. One was adjacent to an arteriole in the intermuscular fibrous tissue, and the other was in an endomysial position. They consisted of five to ten lymphocytes with proliferation of local fibroblasts. No polymorphs, plasma cells, or large mononuclear cells were present. Although small in size, these foci were suggestive of an early rheumatoid reaction.

**Rheumatoid Arthritis and Psoriasis.**—Four cases were associated with psoriasis and only one gave a positive muscle result. In two cases where no histological changes other than non-specific muscle degeneration were found the psoriasis had been present for five and seven years respectively before the onset of the arthritis; in the third case the psoriasis started four years after the onset of the polyarthritis, and this patient also showed no changes in the muscles.

CASE 76.—The fourth patient was a bath attendant, aged 57, who had had psoriasis for 27 years with exacerbations and remissions. Three years before admission, soon after an accident, he developed polyarthritis. He had lost 2 stone in weight since the onset of the arthritis. An attempt to treat him with gold caused the psoriasis to get worse. There was no anaemia and the sedimentation rate was normal. The x-ray appearances were typical of rheumatoid arthritis with secondary osteo-arthritis.

Section of muscle showed degenerative changes with proliferation of nuclei. The vessels were sclerotic. Two foci of rheumatoid type were present in relation to small vessels lying deeply among the muscle fibres. Both showed lymphocytes, plasma cells, and a few phagocytic large mononuclear cells. They were in all respects similar to the smaller foci noted in clinically typical rheumatoid cases.

#### **Rheumatoid Arthritis and Gonococcal Infection.**

None of the seven cases of chronic polyarthritis included in this group showed the histological changes seen in rheumatoid arthritis. All gave a history of a gonococcal urethritis from 12 and 28 years before the onset of the arthritis. In two cases gonococcal arthritis was suggested by the history of pain in and swelling of the heels and sternoclavicular joints, the asymmetry of the joint involvement and the absence of changes in the joints of the hands. The complement fixation test and prostatic massage, however, revealed no evidence of a gonococcal infection. Two cases were typical gonococcal polyarthritis. They both gave a history of a gonococcal urethritis followed within four and six weeks respectively by acute polyarthritis. From all these cases negative results were obtained on biopsy.

#### **CASES OTHER THAN RHEUMATOID ARTHRITIS**

**Still's Disease.**—Of three cases of Still's disease, two failed to show the changes; one case showed highly characteristic round-cell foci in the muscle, and another showed changes in the skin.

**CASE 72.**—A farmer's daughter, aged 21, gave a history of rheumatic fever at the age of 10. After a recurrence at the age of 13 she developed permanent joint changes with marked wasting, flexion deformity, and painful fibrous ankylosis of the elbows, hips, knees, and ankles. She had had four courses of gold without any improvement. Her heart was not involved. There was marked anaemia (haematocrit 35 per cent.), and the sedimentation rate was raised (C.S.S. 55 per cent.). The x-ray appearances of the hands showed rheumatoid changes. A biopsy of the quadriceps showed only non-specific muscle degeneration but no foci. The skin, however, showed the changes described earlier in this paper and depicted in Fig. 2.

**Subacute Rheumatic Infection.**—Four cases of subacute rheumatic infection with cardiac involvement, but with no permanent joint changes, failed to show any changes in the muscles. However, one case with a negative muscle finding showed changes in the skin.

**CASE 21.**—A housewife, aged 37, gave a history of frequent attacks of pharyngitis and tonsillitis at the age of 18. One month after the last attack there was a sudden onset of fever and the appearance of painful swellings in both Achilles tendons. She was treated as a case of

rheumatic fever and hospitalized for six months. She remained quite well for 4 years when she developed another attack of tonsillitis followed by pain and slight swelling of her knees and hands which lasted for six weeks. She remained symptom free for eight years. In 1946 she had another attack of tonsillitis associated with ? erythema nodosum. From that date she began to gain weight, and put on 3 stone in 3 years. On admission she was grossly overweight and presented the features of a case of panniculitis. The joints were not involved. There was a soft systolic murmur at the apex which did not vary with changes of posture, and she had fair tolerance to exercise. The haematocrit was 46 per cent. The sedimentation rate was increased (C.S.S. 78 per cent.), and the plasma uric acid was 3.8 mg. per cent. The skin and subcutaneous tissues were excruciatingly painful and she bruised easily. The muscle was negative but the skin showed the presence of perivascular round-cell foci in relation to the cutaneous vessels, the appearances very similar to those previously noted in skin covering subcutaneous nodules in rheumatoid arthritis.

**Rheumatic Fever.**—One case of a boy, aged 15, suffering from rheumatic fever with gross cardiac enlargement, a double mitral lesion, and multiple subcutaneous nodules did not show the changes in the muscles met with in rheumatoid arthritis.

**Non-specific Infective Arthritis.**—Four cases showing atypical features could not be included in the idiopathic rheumatoid arthritis group and will be described in detail. One case gave positive findings in both muscle and synovia. Two showed changes consistent with rheumatoid arthritis in the synovia but the muscle sections were negative, and in the fourth the muscle was negative but the synovia was not examined.

**CASE 57.**—In 1942 at the age of 29 a housewife, directly after the Bath blitz, noticed a sudden pain and swelling of both her knees. The left knee improved after a few weeks but the right knee became progressively worse. No other joints were affected. In 1945 the right knee was swollen and painful and the synovial membrane appeared thickened. Repeated aspirations produced no improvement. An arthrotomy and knee lavage was performed but with only temporary benefit. In 1945 a synovectomy revealed a very thickened synovium. The haematocrit was 41 per cent. and the blood sedimentation rate was maximal (C.S.S. 62 per cent.).

The section showed an extensive degree of muscle degeneration and fibrosis. Certain areas consisted of dense fibrous tissue with small atrophic muscle fibres still persisting within it. The vessels showed advanced sclerosis. In some of the small arterioles the lumen was almost obliterated. One perimysial focus of round cells was seen. It involved the adventitial coat of a small vessel and consisted of lymphocytes with scanty neutrophil polymorphs and large mononuclear cells. The findings were fully consistent with rheumatoid arthritis.

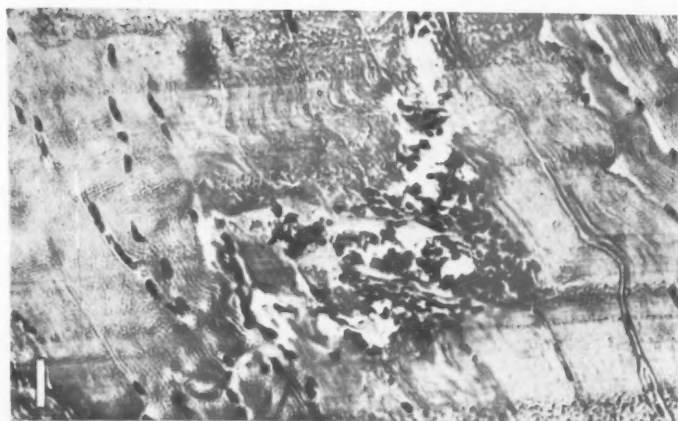


FIG. 1.—Quadriceps muscle from a typical case of idiopathic rheumatoid arthritis showing a perivascular round-cell focus. (Haematoxylin and eosin  $\times 100$ .)

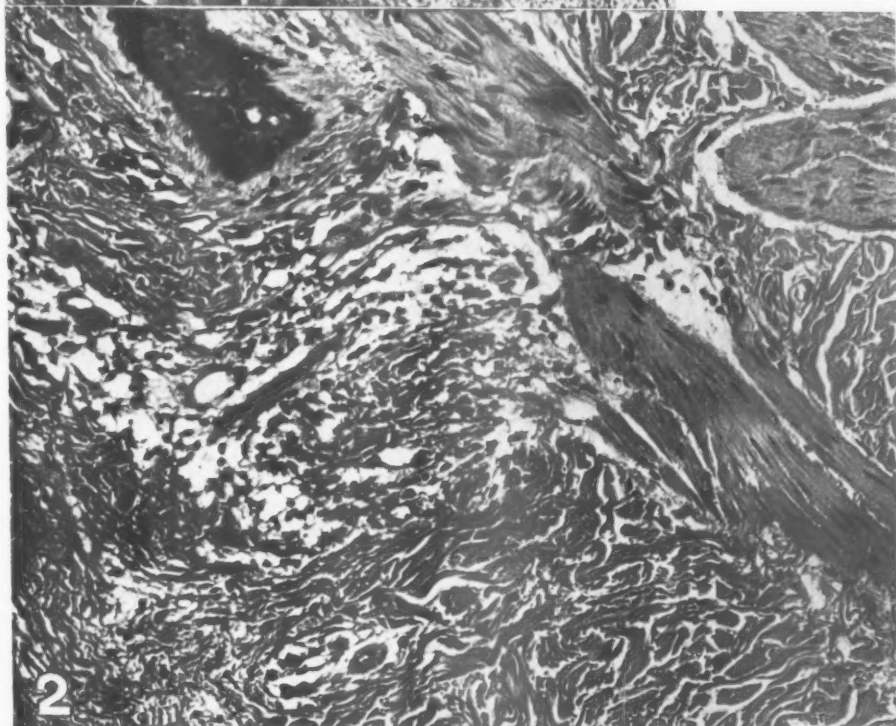


FIG. 2.—Skin from a case of Still's disease. Focus of round-cell reaction involving an erector pilae muscle. (Haematoxylin and eosin  $\times 100$ .)

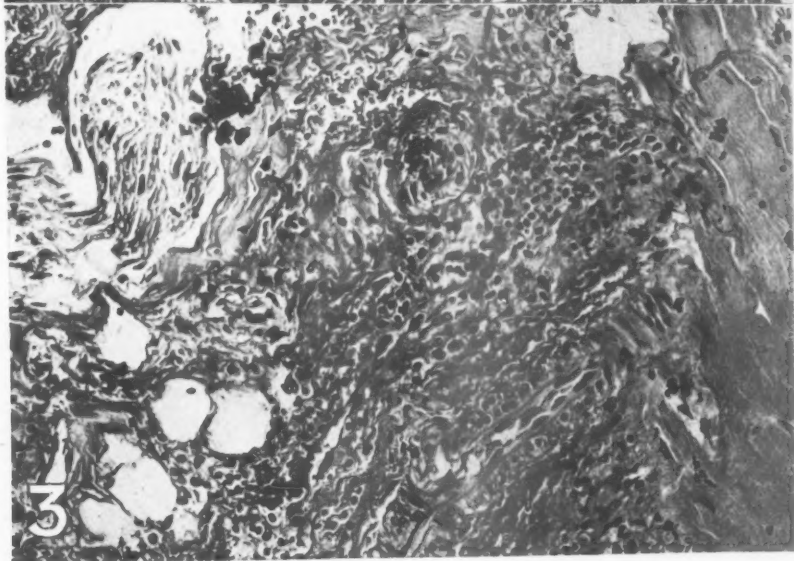


FIG. 3.—Muscle and fibrous tissue from Volkmann's ischaemia showing muscle degeneration with fibrosis with diffuse round-cell infiltration of fibrous tissue. (Haematoxylin and eosin  $\times 100$ .)



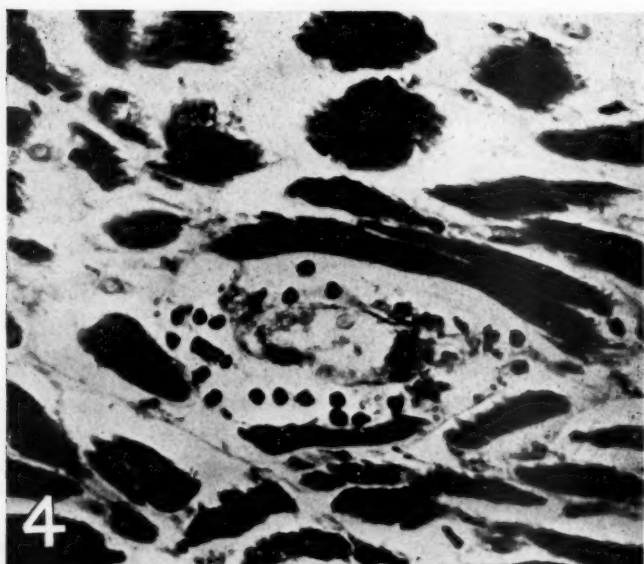


FIG. 4.—Quadriceps muscle from a case of spinal tuberculosis causing paraplegia. Very scanty lymphocytes in relation to vessel. (Haematoxylin and eosin  $\times 400$ .)

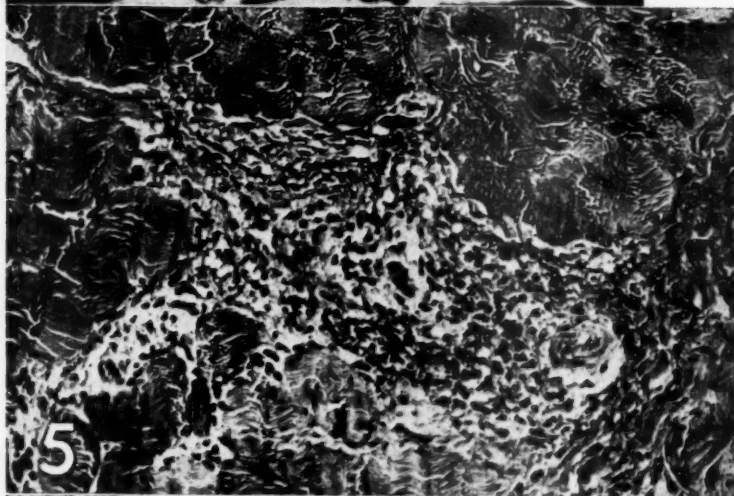


FIG. 5.—Muscle from a case of myositis of unknown origin. No evidence of rheumatism was present. Interstitial round-cell (lymphocytic) infiltration of muscle. (Haematoxylin and eosin  $\times 100$ .)

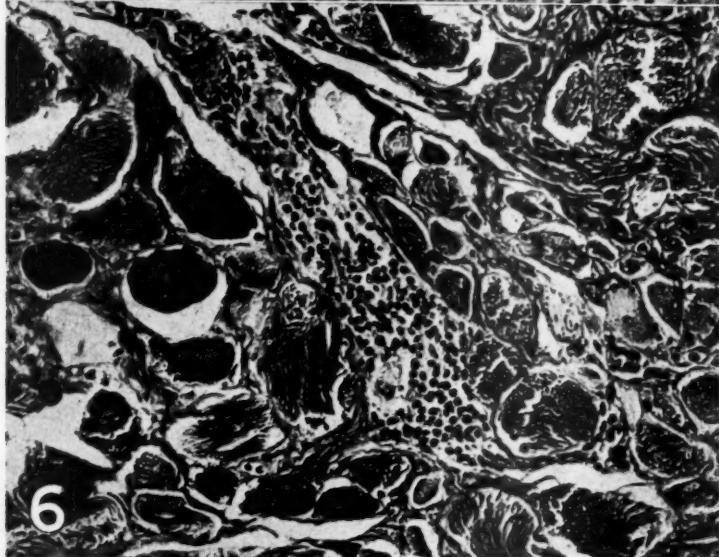


FIG. 6.—Muscle underlying site of foreign-body reaction following removal of breast. Muscle shows degeneration and fibrosis with round-cell reaction simulating that of rheumatoid arthritis. (Haematoxylin and eosin  $\times 100$ .)

**CASE 104.**—In 1943 a male, aged 36, felt a sudden sharp shooting pain in his left hip in stepping off a kerb. The pain seemed to spread all over his body. There was no fever and no sore throat. He was in bed for 19 weeks. The pain and swelling settled in the right ankle and right knee. There had never been any loss of weight and there was no history of past infection. In 1945 the left knee, the feet, and ankles became painful and swollen. His general condition was good but there was marked wasting of the lower right limb. In 1947 the pain and swelling in the knees had become worse. There was marked synovial thickening and a moderate effusion was present. The haematocrit was 35 per cent, and the blood sedimentation rate was maximal (C.S.S. 57 per cent.). Radiographs of the hands, which clinically were not affected, showed changes presumptive of rheumatoid arthritis. A bilateral knee lavage was performed and two specimens of muscle and synovia were excised for examination. Both muscle biopsies failed to show the changes described previously, but the synovial changes were consistent with rheumatoid arthritis.

**CASE 2.**—A male, aged 20, gave a history of gradual onset of swelling of both his knees in 1946. There had been no history of trauma or infection. At about the same time he had experienced pain and swelling of the first metacarpo-phalangeal joints. There was nothing relevant in the family history, and the Kahn reaction was negative. On admission the knees were found to be grossly unstable with bilateral effusion and synovial thickening and moderate wasting of the quadriceps. There was no anaemia, the haematocrit being 42 per cent., and the blood sedimentation rate was normal (C.S.S. 90 per cent.). Radiographs of the hands showed evidence of very early osteoporosis. A bilateral arthrotomy and knee lavage was performed and the specimen of muscle from both vasti showed no changes, but accumulations of lymphocytes were found in the synovia.

**CASE 32.**—A labourer, aged 57, gave a history of an injury to the right hip 15 years ago. In 1944 he was discharged from the Marine Police with arthritis of the right hip. One year later he noticed pain in and limitation of movements of the right shoulder. He was given a full course of gold with moderate improvement. On admission the haematocrit was 41 per cent. and the blood sedimentation rate was maximal (C.S.S. 59 per cent.). The plasma uric acid was 4.7 mg. per cent. Apart from the hip and the right shoulder, all the other joints appeared normal. Radiographs of the hands showed nothing abnormal.

A biopsy from the right vastus externus showed no round-cell foci and no definite evidence of degenerative changes in the muscle.

In addition the following material was seen which, while not sufficiently similar to cause confusion, showed features common to some seen in rheumatoid arthritis. Muscle and synovial membrane collected at operation from a young girl aged 14 with a history of chronic pain and swelling of the right knee of unknown aetiology showed no abnormality in the muscle but changes in the synovia of non-specific type.

**Spondylitis Ankylopoietica.**—Muscle biopsies in seventeen cases of spondylitis ankylopoietica were examined and in all specimens the result was negative.

In three cases the material was collected from the deltoid muscle. There was no muscle wasting in the upper limbs and the shoulders and peripheral joints were not involved. In twelve cases the biopsy was taken from the quadriceps. Of these, five cases showed muscle wasting ranging from slight to very marked degree. The knees and hips were involved in one case.

In seven cases no evidence of quadriceps wasting was present, the condition being limited to the spine and sacro-iliacs only. In two cases the muscle was collected from the erector spinae in the lumbar region, the site most affected.

**Gout.**—Muscles from five cases of typical gout were examined and were negative. The biopsy was taken from the quadriceps in five cases and from the right deltoid in one. Two cases were of advanced tophaceous gout and showed marked quadriceps wasting with involvement of the knee joints. One case which might be considered one of atypical gout showed on biopsy mild degenerative muscle changes only.

**CASE 45.**—A male, aged 36, soon after an attack of pneumonia and pleurisy in 1945 noticed pain in his feet and hands. The proximal interphalangeal joints of the hands were painful and swollen. He had been treated as a case of rheumatoid arthritis and given two courses of gold with only slight improvement. He subsequently developed periodic attacks of pain and slight swelling in the joints of his hands and feet lasting for two or three days. Between the attacks he had always felt perfectly well. On admission his general condition was satisfactory. There was slight muscle wasting of the forearms and the interossei muscles. The epitrochlear glands were enlarged. He had never lost any weight. The joints were symmetrically involved; the knees, hips, and ankles were not affected. The haematocrit had always been normal, and several estimations of the sedimentation rate had given normal figures. The plasma uric acid had fluctuated between 4.4 and 6.7 mg. per cent. X-rays of the hands showed no osteoporosis, but numerous translucent areas of gouty type. He responded well to colchicine therapy. A muscle biopsy from the right vastus externus, which was not wasted, showed mild degenerative muscle changes only. No vascular disease was present and no round-cell foci of rheumatoid type were seen.

**Osteo-Arthritis.**—Seven cases of osteo-arthritis of the hip joint were investigated. In six cases the result was negative, but in one changes were found which were suggestive of a rheumatoid reaction.

CASE 96.—A male, aged 63, with osteo-arthritis changes of the left hip superadded on congenital shortening of the left leg gave no history or clinical evidence of rheumatoid arthritis. There was no anaemia, and the sedimentation rate was normal (C.S.S. 82 per cent.) The plasma uric acid was 6.1 mg. per cent.

On section the muscle fibres showed very slight degenerative changes. The small arterioles had thickened walls but the patient's age might account for this. In two areas in one section examined, but not in further sections made at different levels in the same block, small cellular accumulations were seen. They consisted of large mononuclear cells of endothelial type with a few lymphocytes and some proliferation of local fibrous tissue cells and sarcolemma nuclei. Both were in relation to capillary vessels between the muscle fibres. They were similar in appearance to the smaller foci found in rheumatoid arthritis but were not quite typical.

**Non-rheumatic Cases.**—Muscle from three cases of poliomyelitis failed to show any lesion of the "rheumatoid" type. Degenerative changes and fibrous replacement were the only features to be seen.

Three cases were seen of specific infective arthritis—a streptococcal arthritis of the right knee, a tuberculous arthritis of the knee, and a chronic osteomyelitis. In the latter the muscle examined was adherent to the bone focus and also showed degeneration and fibrosis of varying degrees, but no round-cell foci.

A case of Paget's disease and one of prolapsed intervertebral disc were also negative. A muscle sample taken from the left supraspinatus of a case of fibrositis showed thickening of the fascial covering of the muscle with some sclerosis of the arterioles in the fibrous tissue, but no round-cell foci.

Muscle from a case of Volkmann's ischaemia showed a diffuse round-cell infiltration in the fibrous tissue among muscle fibres. The cells were not related to blood vessels as in rheumatoid arthritis and were scattered throughout the area (Fig. 3).

The quadriceps muscle from a case of tuberculosis of the spine with paraplegia and marked wasting of the lower limbs showed a few lymphocytes in small foci near blood vessels (Fig. 4). This specimen is included here as an example of round-cell reaction in what is probably a purely trophic wasting of muscle.

In a case of chronic myositis of unknown aetiology the muscle fibres were shrunken and atrophic and were surrounded by loose fibrous tissue. Around the vessels there were localized round-cell foci consisting of lymphocytes, plasma cells, and a few polymorphs (Fig. 5).

Two cases were found in which a rheumatoid pathology might have been diagnosed if an isolated field only had been examined.

Following a left mastectomy in a woman, aged 47, a small nodule appeared in the region of the operation scar. Seven months after the first operation, this was excised together with some of the underlying muscle. The main mass consisted of small foreign bodies with accompanying fibrous and giant-cell reaction; "foam cells" and cholesterol clefts were present. In the underlying muscle at some distance from the main nodule there were focal accumulations of lymphocytes resembling closely those seen in rheumatoid arthritis (Fig. 6).

Following a fall seven months previously a woman, aged 52, was admitted with a fusiform, painless swelling over the upper end of the left femur. Biopsy showed fibrosis of the muscle with degeneration and shrinkage of the fibres. The blood vessels showed perivascular round-cell reaction involving the adventitial coat. Certain fields showed round-cell foci among the muscle fibres, in some respects similar to those of rheumatoid arthritis. The cells present were mainly lymphocytes, with a few plasma cells, polymorphs, and large mononuclear cells. This condition was regarded as a post-traumatic chronic inflammatory reaction in the muscle.

Muscle from a case of amyotonia congenita showed the typical histology of that condition, but no round-cell foci were present.

### Discussion

1. No relationship was found between the incidence of positive biopsies and the activity of the arthritis. Lesions were present in cases of from one to twenty-four years' duration, but the chances of finding a typical reaction in the muscles increased with the duration of the disease process.

2. Muscle biopsy appears to be of value in difficult cases. A positive finding would be strongly in favour of a diagnosis of non-specific polyarthritis.

3. The other positive histo-pathological changes in the synovia, skin and subcutaneous nodules, and the reaction taking place in relation to blood vessels of the fibrous supporting tissues suggest that the muscle lesions are only a part of a widely distributed mesodermal reaction.

4. The fact that the lesions were found in apparently healthy muscles not related to affected joints and in such small specimens of muscle selected at random is evidence of the widespread nature of the reaction and also that the muscle lesions were not secondary to muscle wasting or local joint disease. Their absence in cases of specific infective arthritis is evidence that they are probably not secondary to joint disease *per se*.

5. Further evidence that rheumatoid arthritis and



spondylitis ankylopoietica are two different diseases is afforded by the absence of a single positive biopsy in sixteen cases of ankylosing spondylitis.

### Summary

Recent literature on the histo-pathology of non-articular tissue in rheumatoid arthritis is reviewed.

Examination of muscles obtained either by biopsy or at operation was carried out on a series of fifty-six typical cases of idiopathic rheumatoid arthritis, five cases of non-specific infective arthritis, forty-three cases of other rheumatic conditions, and fifteen non-rheumatic controls. Of the fifty-six cases of typical idiopathic rheumatoid arthritis investigated, 34 (60.7 per cent.) showed round-cell foci and thickening of the walls of the blood vessels.

The changes in the muscles were present both in cases in which the disease was active and in those which appeared clinically quiescent or "burnt out".

The lesions were found in cases with and without muscle wasting.

Muscle remote from affected joints also showed the typical lesions.

No typical rheumatoid changes were found in cases of less than six months' duration. In those examined within three years, seven years, and from eight years onwards the chances of finding the lesions were 47 per cent., 60 per cent., and 82 per cent. respectively.

Seventeen out of the thirty-four cases of typical idiopathic rheumatoid arthritis with positive muscle findings showed other positive histological changes either in the synovia, skin, or subcutaneous nodules. Four cases with negative findings in the muscle showed typical changes in other mesodermal tissues.

Of four cases of rheumatoid arthritis associated with psoriasis, one case gave a positive muscle finding.

Five cases of chronic polyarthritis with a past history of a gonococcal urethritis, and two cases of typical gonococcal arthritis all gave negative results on biopsy.

Of three cases of Still's disease, two failed to show muscle changes; one case showed highly characteristic round-cell foci, and another showed lesions in the skin.

Lesions were found in the muscles in one out of four cases of rheumatoid arthritis with a past history of rheumatic fever.

Four cases of subacute rheumatic infection with a past history of rheumatic fever gave negative muscle findings. One case, however, showed changes in the skin.

One case of rheumatic fever showed no change in the muscles.

The muscle lesion was found in one of five cases of non-specific infective arthritis. The synovia in three of these cases showed changes consistent with rheumatoid arthritis.

Muscle biopsies in seventeen cases of spondylitis ankylopoietica were examined. All gave negative results.

Muscle examined from six cases of typical gout were all negative.

Seven cases of osteo-arthritis of the hip joint were examined. In six the results were negative, but in one case changes were found which were suggestive of a rheumatoid reaction.

Muscle from fifteen non-rheumatic controls were examined. This group consisted of the following cases: three of poliomyelitis; three of specific infective arthritis; one of Paget's disease; one of prolapsed intervertebral disc; one of fibrositis. All these cases gave negative results.

Among cases showing lesions in muscle which resembled in some respects those seen in rheumatoid arthritis were one example each of the following conditions: Volkmann's ischaemia; atrophic muscle following tuberculosis of the spine, with paraplegia; chronic myositis of unknown origin; breast tumour showing foreign-body reaction; post-traumatic myositis.

We should like to express our thanks to the Sidney Robinson Research Fund for assistance in defraying expenses in connexion with this work, to the remainder of hospital staff of the Royal National Hospital for Rheumatic Diseases for giving us access to cases under their care, and in particular to Mr. Bastow for supplying us with material from cases operated on at other hospitals.

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### Histologie du Muscle chez des Rhumatisants et des Sujets Normaux

#### RÉSUMÉ

Les auteurs passent en revue les publications récentes sur l'histologie pathologique des tissus articulaires dans l'arthrite rhumatismale.

Des muscles obtenus soit par biopsie soit à la suite d'opérations ont été examinés sur une série de cinquante-six cas d'arthrite rhumatismale idiopathique typique, cinq cas d'arthrite infectieuse non spécifique, et quarante-trois cas d'autres affections rhumatismales, et sur quinze sujets non rhumatisants. Sur les cinquante-six cas d'arthrite rhumatismale idiopathique typique, 34 (60.7 pour cent) présentaient des foyers globo-cellulaires et un épaississement des parois vasculaires.

Les altérations musculaires étaient présentes aussi bien dans les cas où la maladie était en pleine activité que dans ceux où elle semblait cliniquement latente.

On a observé ces lésions aussi bien chez les sujets atteints d'atrophie musculaire que chez ceux qui n'en présentaient pas.

Ces lésions typiques étaient également présentes sur les biopsies pratiquées loin des articulations atteintes.

On n'a observé aucune altération rhumatismale typique chez les sujets atteints depuis moins de six mois. Chez les sujets étudiés au bout de trois ans, sept ans, et huit ans et au-delà, les chances de trouver des lésions étaient respectivement 47, 60, et 82 pour cent.

Sur les trente-quatre cas d'arthrite rhumatismale idiopathique typique avec lésions musculaires, dix-sept présentaient d'autres lésions histologiques positives de la membrane synoviale, de la peau, ou des nodules sous-cutanés. Quatre cas sans lésions musculaires présentaient des altérations typiques d'autres tissus d'origine mésodermique.

Sur quatre cas d'arthrite rhumatismale accompagnée de psoriasis, un seul cas présentait des lésions musculaires.

Cinq cas de polyarthrite chronique avec des antécédents d'urétrite gonococcique, et deux cas d'arthrite gonococcique typique ont tous donné des biopsies négatives.

Sur trois cas de syndrome de Still-Felty, deux ne présentaient aucune lésion musculaire; un seul pré-

sentait des foyers globo-cellulaires nettement caractéristiques, et un autre des lésions cutanées.

Sur quatre cas d'arthrite rhumatismale avec antécédents de rhumatisme articulaire aigu, on n'a trouvé de lésions musculaires que dans un seul cas.

Quatre cas d'infection rhumatismale subaiguë avec antécédents de rhumatisme articulaire aigu ont donné des résultats négatifs. L'un des malades présentait cependant des lésions cutanées.

Un cas de rhumatisme articulaire aigu ne présentait aucune lésion musculaire.

On a observé la lésion musculaire typique dans un cas d'arthrite infectieuse non spécifique sur cinq étudiés. Chez trois de ces sujets la membrane synoviale présentait des modifications cohérentes avec l'arthrite rhumatismale.

Les examens de biopsies de muscles dans dix-sept cas de spondylite ankylosante ont tous donné des résultats négatifs.

Six cas de goutte n'ont présenté aucune lésion musculaire.

On a étudié sept cas d'arthrite ostéo-articulaire de la hanche. Six ont donné des résultats négatifs mais on a trouvé chez un malade des lésions suggérant une réaction rhumatismale.

On a examiné des muscles de quinze sujets témoins non rhumatisants. Ce groupe était constitué par les cas suivants: trois cas de poliomyélite; trois cas d'arthrite spécifique infectieuse; un cas de maladie de Paget; un cas de déplacement de disque intervertébral; un cas de cellulite. Tous ont donné des résultats négatifs.

Parmi les sujets qui présentent des lésions musculaires ressemblant de près ou de loin à celles de l'arthrite rhumatismale, se trouvait un exemple de chacune des affections suivantes: paralysie ischémique de Volkmann; atrophie musculaire après tuberculose vertébrale, avec paraplégie; myosite chronique d'origine inconnue; tumeur du sein simulant un corps étranger; myosite post-traumatique.

# BAL IN THE TREATMENT OF GOLD TOXICITY

BY

J. G. MACLEOD

*From the Department of Medicine, University of Edinburgh*

Gold is generally regarded as a useful therapeutic agent in the treatment of rheumatoid arthritis. Unfortunately its administration, however carefully supervised, is attended by the risk of various toxic reactions, some of which may be fatal. Until the introduction of BAL, no specific treatment was available for such toxic reactions. Favourable results with this drug have lately been reported from America in twenty cases described by various authors, and in three cases in this country.

Research carried out by Peters and his colleagues (1945) led to the discovery of BAL, and to its use as a therapeutic agent in the treatment of toxic reactions to heavy metals. Further experimental work carried out in America confirmed and elaborated the findings of these workers (Waters and Stock, 1945). Essentially, BAL acts by competing with tissue cells for certain metals. It forms with the metal a stable compound which is as a rule non-toxic and which is believed to be rapidly excreted. BAL proved highly successful in the prevention and treatment of lewisite burns (Stocken and Thompson, 1941; Vey, 1941); in the treatment of the complications of arseno-therapy (Carleton and others, 1946; Longcope and others, 1946); and in the treatment of acute mercury poisoning (Longcope and Luetscher, 1946). The experimental work of Long and Farah (1946) suggests that it may be of use in severe reactions due to mercurial diuretics. BAL may also be found to be effective in poisoning due to the inhalation of zinc fumes (Annotation, *Nature*, 1946), and may have an application in veterinary medicine in diseases of copper metabolism in sheep (McDonald, 1946).

Among the first papers on the use of BAL in toxic reactions due to gold was that of Ragan and Boots (1947). Before using the drug in human subjects suffering from gold toxicity these authors carried out an important preliminary experiment. While BAL combines with heavy metals to form a compound that as a rule is non-toxic, that compound formed with cadmium causes acute nephritis. Ragan and Boots demonstrated that animals

treated simultaneously with gold and BAL showed no toxic effects in heart, liver, or kidney. BAL was then used in five cases of rheumatoid arthritis with gold dermatitis in man, with a good result in four instances. In all cases a significant increase in the urinary excretion of gold occurred coincident with the administration of BAL. Four patients had an exacerbation in symptoms due to rheumatoid arthritis within one month of this treatment. Cohen and others (1947) reported five cases, three with gold dermatitis, one with pruritus and conjunctivitis, and one with stomatitis, treated successfully with BAL. Margolis and Caplan (1947) found BAL of benefit in one case of severe stomatitis and in one case of mild conjunctivitis, anal ulceration, and dermatitis; they claimed amelioration of long-standing exfoliative dermatitis in two cases; in one case of mild dermatitis no appreciable benefit was obtained. Margolis and Caplan concluded that the early use of BAL in the treatment of toxic effects resulting from the administration of gold appeared to be of value. Davison (1947) successfully treated three early cases of gold dermatitis. Lockie and others (1947) obtained a spectacular recovery in two serious reactions to gold; one reaction was thrombocytopenic purpura, and the other agranulocytosis. In this country three cases of gold dermatitis have been treated successfully with BAL (Slot and McDonald, 1947; Simpson, 1948).

In the present paper the results of the use of BAL in fifteen cases of gold toxicity are described; the series includes two cases of acute hepatitis due to gold, in which condition its use has not hitherto been reported.

### Clinical Findings in the Present Series

The fifteen cases in the present series consist of eleven patients with dermatitis; two of these had stomatitis in addition. In one case stomatitis was the only toxic reaction. Two patients had acute hepatitis and one had hypoplastic anaemia.



A summary of each case is given in the Table. In addition four sample cases are described more fully to expand and illustrate the Table. One case of dermatitis, one of dermatitis and stomatitis, and two of hepatitis have been chosen for this purpose. It was felt that a fuller description of the two patients suffering from hepatitis would be of special interest as toxic reactions of this type have not previously been described treated with BAL.

### Case Records

**Case 1.**—A married woman, aged 39 years and weighing 70 kg., who had suffered from rheumatoid arthritis since November, 1946, received 0.58 g. of myochrysine. The last five doses were of 0.1 g., and the final dose was given on June 11, 1947. Dermatitis developed on June 18, and by June 30 was of a generalized exfoliative nature and still spreading. On that day treatment with BAL was commenced in successive daily doses of 400 mg., 200 mg., 200 mg., 200 mg., 100 mg., and 100 mg. intramuscularly. Individual doses were of 100 mg. There were no toxic reactions, and forty-eight hours after the commencement of treatment improvement was present, best seen in diminished swelling of the face. There was also a marked decrease in pruritus. Steady improvement continued until July 21, when the only finding was a few non-irritant papules on the legs. A slight exacerbation in the following week subsided spontaneously. On Sept. 13 a scaly eruption the size of a halfpenny was present on the dorsum of the left foot, and this had disappeared by Nov. 15. When the patient was last seen on the latter date there had been no recurrence of arthritic symptoms.

**Case 10.**—An unmarried woman, aged 24 years and weighing 63 kg., who had had rheumatoid arthritis for eighteen months, was treated with 0.68 g. of myochrysine. The last six doses were of 0.1 g. and the last injection was given on July 20, 1947. On July 6, 1947, a sore mouth developed, followed by ulcers of the tongue and gums and on July 20 by an itching rash on the hands. The patient was admitted to hospital on July 21 with severe stomatitis and moderate dermatitis of the hands. On July 23 dermatitis was present on the anterior aspect of both legs.

On July 25 both conditions were deteriorating, and on successive days BAL was given intramuscularly in doses of 400 mg., 200 mg., 200 mg., 200 mg., 100 mg., and 100 mg. Transient local pain and nausea followed the earlier injections of BAL, but twenty-four hours after the first injection the patient announced she was "better", and forty-eight hours afterwards reported that the soreness of the mouth was less and that the itch had gone. By July 28 the dermatitis was less extensive and less erythematous, and the ulcers of the mouth were healing. When the patient was discharged on Aug. 3 the stomatitis was healed and some desquamation of the right palm was the only residual evidence of dermatitis. On Aug. 16 this was still evident, and one small ulcer was present in the mouth. On Oct. 11 there was no dermatitis or stomatitis and no residual pigmentation. On

Nov. 15 there was no evidence of any relapse in the rheumatoid arthritis.

**Case 13.**—A married woman, aged 51 years and weighing 47 kg., had suffered from rheumatic mitral stenosis, auricular fibrillation, and intermittent attacks of congestive heart failure for three years; rheumatoid arthritis had been present for about the same length of time; symptoms from the arthritis were severe and treatment with myochrysine was begun on Oct. 14, 1947. By 12 Dec. 0.38 g. had been given, with an improvement in the arthritis; the largest dose administered was 0.05 g. On Dec. 17 the patient complained of having felt profoundly exhausted for two or three days. She gave the appearance of being a seriously ill woman. A slight icteric tinge was present and the urine contained urobilinogen in excess. The liver was not enlarged. The icteric index was 17 units (Meulengracht). Gold hepatitis was diagnosed, and on Dec. 18 treatment with BAL was begun in successive daily doses of 200 mg., 300 mg., 300 mg., 300 mg., and 200 mg. There were no local reactions, but immediately after the last injection the patient complained of nausea, epigastric discomfort, and some diarrhoea. BAL was stopped, and symptoms subsided within twenty-four hours.

Within forty-eight hours of the first injection there was marked subjective and objective improvement. Tiredness was less, and the icteric tinge disappeared. Urobilinogen was present in the urine in excess until Dec. 21, that is, four days after the commencement of BAL. On and after that date urobilinogen could no longer be demonstrated. The icteric index was unfortunately not repeated until Jan. 5, 1948, when the reading was 8 units. At this time the serum albumin was 3 g. per cent. and the serum globulin 2.8 g. per cent.

The patient remained well until Jan. 19, when tiredness and drowsiness returned. Her temperature rose to 102° F., and she complained of frequency of micturition and dysuria. The urine contained numerous pus cells, and a profuse growth of *B. coli* was obtained on culture. The icteric index was 9 units. Treatment with sulphanilamide, 1 g. thrice daily, was begun. On Jan. 21 the urine contained urobilinogen in excess and the icteric index was 15 units. Next day 300 mg. of BAL, and on 23 Jan. 200 mg. were injected in doses of 100 mg. Severe abdominal pain, intense nausea, and repeated vomiting followed the injections of BAL, which had to be stopped with resultant improvement in the abdominal symptoms by the following day—Jan. 24. On this date the urine contained no pus but urobilinogen in excess. Though the vomiting had ceased the patient's general condition was still very poor. She was tired, drowsy, and had a yellowish, muddy complexion. The liver was two finger-breadths enlarged; the icteric index was 34 units. On Jan. 27 drowsiness was extreme, the patient was irresponsive, and at noon the prognosis appeared hopeless. BAL, 100 mg., was injected at 3 p.m. and 4 p.m. Following the second dose there was improvement; she was less drowsy, replied to questions, and admitted an improvement. This continued slowly over the next few days: 100 mg. BAL was given on Jan. 28 and 30, and from Feb. 2 to 7 inclusive. On Feb. 4 the icteric index was 22 units. By Feb. 6 there

TABLE  
DETAILS OF FIFTEEN CASES OF GOLD TOXICITY TREATED WITH BAL

Case	Age yrs.	Wt. kg.	Diagnosis	Total dose gold (g.)	Toxic effects	Delay in therapy	Dose of BAL (mg.)	Toxic effects of BAL	Result	Follow-up	Relapse in R.A.
1	39	70	R.A.	0.58	Exfoliative dermatitis	12 D	1,200 in 6 D	0	Decrease in pruritus within 48 hours. Progressive regression in dermatitis. No further lesions. Only minimal resi- dium in 3 W. No residual pig- mentation.	5 M	0
2	53	60	R.A.	0.38	Dermatitis (general- ized)	4 W	1,200 in 6 D	0	Pruritus less in 2 D and almost nil in 4. Dermatitis much less erythematous and less extensive in 6 D; more scaly. No more lesions. Hyperkeratosis of skin persisted for about 3 M. No residual pigmentation.	5 M	0
3	49	68	Osteo- arthritis	0.88	Dermatitis (general- ized)	3 M	1,200 in 4 D	0	Slight improvement within 1 W, by which time rash had changed in character all areas, now marked follicular hyper- keratosis. Hair ceased coming out. Skin quiescent 6 W later. No further lesions. Pigmenta- tion minimal.	6 W	N.A.
4	39	70	R.A.	0.75	Dermatitis (general- ized)	1 M	1,200 in 6 D	Anorexia for 1 W. Urticaria at site of inject. 19 D after BAL. Con- trolled by Benadryl	Two W later no itch, less ery- thema, plaques smaller. No further lesions. When seen after 2 M, skin virtually healed.	2 M	Return of joint pains

R.A. = Rheumatoid Arthritis; M = month; W = week; D = day.

TABLE (continued)

Case	Age yrs.	Wt. kg.	Diagnosis	Total dose gold (g.)	Toxic effects	Delay in therapy	Dose of BAL (mg.)	Toxic effects of BAL	Result	Follow-up	Relapse in R.A.
5	29	60	R.A.	0.58	Dermatitis (general- ized)	2 M	1,200 in 3 D		Free from pruritus in 3 D. Steady decrease in extent of dermatitis. No further lesions. Change to appearance of follicular hyperkeratosis within 10 D. For 1 M some dermatitis still present but still decreasing and appeared quiescent.	1 M	0
6	50	77	R.A.	1	Pruritus (severe)	2 W	100 in 1 D as O.P.	0	One W later reported marked and maintained decrease in itch.	7 M	0
7	63	65	R.A. Benign hyperten- sion	0.75	Dermatitis limbs (mild)	4 M	200 in 1 in- ject. as O.P.	0	Two W later severe pruritus had disappeared. Dermatitis less extensive and more quiescent.	0	
8	47	77	R.A.	1	Dermatitis buttocks (mild)	8 W	300 in 1 in- ject. as O.P.	Numbness of legs for 2 D. Las- situde for 4 D	Pruritus absent in 4 D. Dermatitis less extensive, less erythematous and more scaly in 1 W.	0	
9*	57	75	R.A.	0.93	Dermatitis limbs (mild)	4 M	300 in 1 in- ject. as O.P.	0	Two W later dictator reported: "No further spread and no new lesions. Apparent healing. No itch."	0	
10	24	63	R.A.	0.68	Dermatitis limbs: stomatitis severe	19 D	1,200 in 6 D	Minimal local pain and nausea	Disappearance of pruritus in 2 D. Dermatitis less extensive and less erythematous in 3 D. No further lesions. Desquamation of palms only in 9 D. Skin healed in 2-3 M. No residual pigmentation. Stomatitis healed in 9 D.	4 M	0
11	59	44	R.A.	0.47	Dermatitis (general- ized): stomatitis slight	1 W  2 M	1,200 in 3 D	Local pain and nausea after initial injection only	Dermatitis. Decrease of pruritus and apparent regression of dermatitis in 3 D. Relapse 4 D later controlled by 150 mg., 200 mg., and 150 mg. BAL at weekly intervals as O.P. Stomatitis. Improvement in 3 D. Minor relapse healed rapidly.	1 M	0

R.A. = Rheumatoid Arthritis; M = month; W = week; D = day.

\* All the patients except Case 9 were women.



TABLE (continued)

Case	Age yrs.	Wt. kg.	Diagnosis	Total dose gold (g.)	Toxic effects	Delay in therapy	Dose of BAL (mg.)	Toxic effects of BAL	Result	Follow-up	Relapse in R.A.
12†	47	60	R.A.	0.68	Stomatitis	0	1,200 in 6 D	0	No further lesions after 24 hours. Less pain in 2 D. Progressive healing, complete in 1 W.	0	
13	51	47	R.A. Mitral stenosis Pyelo- nephritis	0.38	Hepatitis	5 D	1,300 in 5 D	Nausea, epigastric pain, and diarrhoea subsiding on stop- ping BAL	Marked improvement in 48 hours. Urobilinogen disappeared from urine in 4 D. Icteric Index fell from 17 to 8 units.	4 M	0
					Relapse of hepatitis 1 M later	0	500 in 2 D	Nausea, vomiting and severe abdominal pain	No improvement.		
14	60	59	R.A.	0.6 g. in 3 doses	Hepatitis	10 D	4 D	0	Immediate dramatic improve- ment. Urobilinogen disap- peared from urine in 8 D. Icteric index fell from 34 to 13 units in 14 D.	2 M	0
							1,000 in 4 D 1 W later 1,200 in 4 D	Minor local pain only 0	Immediate improvement in ano- rexia and lassitude. Urobili- nogen in urine decreased to nil in 2 W. Icteric index fell from 18 to 8 units in 10 D.	1 M	0
15	34	58	R.A. Bronchiec- tasis	6 courses; last 0.08 g. only	Hypoplastic anaemia	10 M	750 in 4 D	Pyrexia might be due to bronchi- ectasis	No significant change in peri- pheral blood or bone marrow before or after BAL.	3 M	0

R.A. = Rheumatoid Arthritis; M = month; W = week; D = day.

† This patient was first seen in the healing stage.

was no excess urobilinogen in the urine, and this finding persisted. By this time the patient's general condition was very much improved. On Feb. 9, 1948, the icteric index was 13 units, the gold sol test positive (2), and plasma proteins were albumin 2.6 g. per cent. and globulin 2.9 g. per cent. On March 1 the patient was allowed up, and by March 27 had shown no relapse in the rheumatoid arthritis. The joints, indeed, continued to show a steady improvement.

**Case 14.**—A married woman, aged 60 years and weighing 59 kg., had suffered from rheumatoid arthritis for two years. A course of myochrysine was begun on Jan. 2, 1948. As a result of a dispenser's error she had on successive weeks 0.1 g., 0.2 g., and 0.3 g., the last being given on Jan. 16. When seen on Jan. 24 she complained of severe nausea, anorexia, and extreme exhaustion. The liver was not enlarged but the icteric index was 18 units and the urine contained urobilinogen in excess. BAL was begun on that day, and on successive days 200 mg., 300 mg., 300 mg., and 200 mg. were given in doses of 100 mg. The patient's symptoms showed prompt improvement and the quantity of urobilinogen in the urine decreased. The icteric index on Jan. 28 was 12 units. On Jan. 30 it was 9 units, and the cephalin flocculation test was positive. As she continued to show a small excess of urobilinogen in the urine, and in view of the relapse that had occurred in Case 13, a second course of BAL, 300 mg. daily, was given from Feb. 3 to 6 inclusive. On Feb. 3 the icteric index was 8 units, and by Feb. 7 the urine contained no urobilinogen. The patient had no complaints. The symptoms due to the arthritis had disappeared, and when she was seen again on Feb. 8 there had been no relapse either in the arthritis or the hepatitis. The icteric index on that date was 10 units, the cephalin flocculation test negative, the serum albumin 4.66 g. per cent., and the serum globulin 2 g. per cent.

### Discussion

**Dermatitis.**—From the results obtained in the eleven cases of gold dermatitis it may be concluded that BAL probably influenced favourably the course of gold dermatitis. A constant finding was the immediate decrease in pruritus. In many cases this disappeared within a few days of commencing the drug. It is more difficult to assess the effect of BAL on the actual eruption. In only one case was the eruption severe. In many of the cases it was mild, and might have been expected to have cleared up spontaneously in a matter of two or three months at the most. On the other hand, although there was no uniform immediate dramatic change in the course of the dermatitis, a steady improvement was evident in all cases in the weeks following the administration of BAL. In only one case did fresh lesions appear after the drug had been prescribed. Further studies in conjunction with the Department of Dermatology are in progress in an attempt to assess the effect of BAL on the course of the dermatitis. It is noteworthy that in the present series

improvement in pruritus and in the course of the eruption was not confined to early cases.

**Stomatitis.**—The three cases of ulcerative stomatitis, one of which was very mild, rapidly healed while under treatment with BAL. In the severer cases there was an immediate and striking improvement in local pain.

**Hepatitis.**—In acute hepatitis a gratifying response was obtained in the two cases treated. In the case which relapsed it may fairly be claimed that BAL proved life-saving. The toxic reactions due to BAL that occur in cases of hepatitis are discussed later.

**Hypoplastic Anaemia.**—No improvement was obtained in one case of hypoplastic anaemia due to gold. The interval between the course of gold and the administration of BAL was ten months. It is known that gold may continue to be excreted in the urine for many months after its administration (Freyberg and others, 1941). It was for this reason that BAL was tried, on the assumption that the minute quantity of gold still presumably present might be enough to depress the bone marrow, and its removal by BAL might result in improvement. No change in the peripheral blood or bone marrow was evident after the administration of BAL. Presumably gold had caused irreversible changes in the marrow.

**Toxic Reactions to BAL.**—The dosage initially used was that recommended by Peters and his colleagues (1947) for adults of average weight, 400 mg. on the first day, 200 mg. on the second, third, and fourth days, and 100 mg. on the fifth and sixth days. Few toxic reactions were encountered in the present series with this dosage, and as experience was gained the dose was increased. Experimental work, mainly on human volunteers, has been carried out by Sulzberger and others (1946), and by Modell and others (1946). These authors showed that up to 5 mg. BAL per kilo of body weight can be given with minimal or no toxic effects, and that in doses up to 8 mg. per kilo the effects are transitory. Toxic effects produced by this dosage usually begin about twenty minutes after the injection, with a return to normal in from forty-five minutes to two hours. Among the toxic effects produced are various paraesthesiae, lacrimation, blepharo-spasm, nausea, abdominal pain, vomiting, unrest, exhaustion, and a transient rise in blood pressure. Local pain at the site of the injection is frequently encountered. Though sensitization of the skin is common in cases where BAL is applied locally, sensitivity reactions in the skin have not followed intramuscular injections. Sulzberger and others (1946) produced skin sensitization as demonstrated by positive patch tests in five of

eighteen subjects. In four of these patients later intramuscular injection of BAL did not produce any cutaneous reactions. Abscesses at the site of injection have been reported by Cohen and others (1947) in cases of dermatitis.

In the present series single doses of up to 4 mg. per kilo body weight have been given with only transient discomfort, mainly in the form of pain at the site of injection. With subsequent injections this often became less marked. In no case did an abscess develop. In one case (No. 4) skin sensitivity developed at the site of injection but this was readily controlled by benadryl.

In one of the cases of hepatitis severe toxic reactions followed the administration of BAL. This is in keeping with the conclusions of Cameron and others (1947). These authors produced renal or hepatic damage in experimental animals, and then administered BAL. They found that full doses of the drug could be given safely in the presence of severe kidney damage, but that in the presence of impaired liver function BAL must be given cautiously, as toxic reactions of variable severity, and even fatalities, resulted from doses well below the fatal level for normal animals. In cases of gold hepatitis it is almost certainly unwise in single doses to exceed 3 mg. of BAL per kilo of body weight, and sometimes even smaller doses may be necessary.

It may be concluded, therefore, that in cases of gold toxicity, other than hepatitis, BAL may be administered in single doses of up to 4 mg. per kilo of body weight with minimal toxic reactions, and that such as occur will subside rapidly within one or at the most two hours. Such single large doses of BAL may therefore be given to out patients with equanimity provided the patient is kept under observation for about one hour after the injection. BAL used in this way may have a useful clinical application which will be discussed later.

**Relapse in Rheumatoid Arthritis.**—It has already been noted that Ragan and Boots (1947) found that four of their five cases showed an increase in the symptoms of rheumatoid arthritis within one month of treatment with BAL. In the present series six cases have been followed up for periods of one to six months and only one of these showed any relapse. This patient had previously relapsed following a course of gold without BAL.

**Excretion of Gold.**—The urinary excretion of gold was estimated by Dr. Crawford in the Department of Pharmacology, in three of the above cases using the method of Block and Buchanan (1940). This was the method used by Ragan and Boots (1947), when they showed an increase in the urinary excretion of gold coincident with the administration

of BAL. In the three cases of the present series where this was estimated there was no such definite increase. It was noted, however, that the results by this method proved unsatisfactory as judged by the estimation of duplicate samples. We have, therefore, no further evidence as to whether the excretion of gold in the urine is or is not increased. The test is difficult and time-consuming, and it is felt that the inaccurate results obtained in our hands are worth noting.

**Dosage of BAL.**—Though relapse in the symptoms of rheumatoid arthritis following treatment with BAL has not been a feature of the present cases, it is probably undesirable for several reasons to use BAL in quantities larger than necessary to control the toxic symptoms. In the first place, though BAL has not resulted in an increase in the symptoms of rheumatoid arthritis in the present series, the experience of others has led to a different conclusion, and a larger series of cases may prove relapse in the rheumatoid arthritis to be a frequent undesirable sequel to BAL therapy. On theoretical grounds relapse would be expected if BAL resulted in an increase in urinary excretion of gold. Secondly, it is well known that cases of rheumatoid arthritis developing toxicity often show a very good improvement in the joint symptoms. Over-treatment of the toxic reactions may therefore be undesirable. Lastly, gold toxicity is usually insidious in its onset; the risk is that it may progress to a dangerous degree, for example, from mild dermatitis to severe exfoliation, or from mild hepatitis to acute yellow atrophy. If the toxic reaction can be controlled at an early stage such danger may be averted and the beneficial effect of gold on the joints be allowed to continue.

It has been shown that BAL may safely be administered to out patients. It is suggested, therefore, on the first sign of gold toxicity, other than hepatitis, and persisting in spite of stopping gold, that BAL may be given in a single intramuscular injection of up to 4 mg. per kilo of body weight in the hope that this will control the toxicity without unduly interfering with the therapeutic effect of the metal. The case can be reviewed from week to week or at shorter intervals, and further single injections of BAL may be given if necessary. BAL has been used in this way effectively in four cases in the present series (Nos. 6 to 9), and further trials are being continued along the same lines.

Where severe toxicity is present, such as exfoliative dermatitis, ulcerative stomatitis, and probably nephritis, agranulocytosis, and thrombocytopenic purpura, more energetic treatment will be required. Work by Wexler and others (1946) on arsenic



poisoning suggested that four-hourly dosage would result in a maintained excretion of that metal. If there is any parallel in gold toxicity, a similar interval between doses is possibly indicated. Such an interval between injections would allow ample time for any reaction to subside and be assessed before the treatment is continued. Sulzberger and others (1946) have shown that no cumulative effects occur in doses up to 5 mg. per kilo at four-hourly intervals. In the cases instanced above, BAL could probably be administered with advantage in quantities up to 4 mg. per kilo of body weight at four-hourly intervals, omitting the night dose, for two or three days according to the improvement obtained. Amounts as large as these have not been repeated at such short intervals in the present series, but trials with this dosage are in progress. It is suggested that 3 mg. per kilo at six-hourly intervals for three or four days would be an adequate and safe dose for cases demanding energetic treatment, such as those under discussion. The work of Sulzberger and others (1946) suggests that, if necessary, a second course of BAL can be given without danger of sensitivity. No ill effects were noted in the present series in the three cases in which additional doses or courses of BAL were administered (Nos. 11, 13, and 14). Weatherall (1948) has pointed out that prolonged treatment with BAL may be dangerous. Cats treated in this way developed anorexia, loss of weight, and a rise in the non-protein nitrogen of the blood (Modell and others, 1946). In the short courses recommended such reactions are unlikely, and they were not encountered in this series.

#### Summary and Conclusions

Previous work on BAL with particular reference to its use in patients suffering from toxic reactions to gold is reviewed. The use of BAL in fifteen such cases is described.

BAL appears to be of value in the treatment of gold toxicity. In dermatitis the immediate improvement in the pruritus is a constant and striking feature, and the course of the eruption is probably influenced in a favourable manner. BAL is also effective in the treatment of stomatitis and hepatitis due to gold.

Toxic effects are minimal in doses up to four milligrammes per kilogramme of body weight, except in cases of hepatitis—in which it is confirmed that BAL must be given in smaller doses if severe reactions are to be avoided.

Relapse of symptoms due to rheumatoid arthritis following the administration of BAL was not a feature of the present series.

No conclusion could be made about the excretion of gold in the urine following BAL therapy.

Recommendations are made about the dosage, partly from a consideration of the previous literature on the subject, and partly from the limited experience obtained in the present series of cases. A distinction is drawn between the use of the drug in the treatment of mild and severe toxic reactions.

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### Le BAL (British Anti-Lewisite) dans le Traitement de l'Intolérance à l'Or

#### RÉSUMÉ ET CONCLUSIONS

L'auteur passe en revue les recherches antérieures sur le BAL (*B*-chlorovinyldichlorarsine) et particulièrement celles qui ont trait à son utilisation chez les malades présentant des signes d'intolérance au traitement par l'or. Il décrit l'utilisation du BAL dans quinze cas de ce genre.

Le BAL semble être actif dans le traitement de l'intolérance à l'or. Dans la dermatite un trait marquant et constant est l'atténuation immédiate du prurit, et l'évolution de l'éruption est influencée dans un sens favorable. Le BAL est également actif dans le traitement de la stomatite et de l'hépatite provoquées par l'or.

Les réactions toxiques au BAL sont faibles pour des

doSES allant jusqu'à quatre milligrammes par kilogramme, excepté dans les cas d'hépatite pour laquelle il a été confirmé que le BAL doit être administré à des doses plus faibles si l'on veut éviter les réactions graves.

Dans la série citée ici on n'a pas constaté que l'administration de BAL ait fait réapparaître les symptômes d'arthrite rhumatismale.

On n'a pu aboutir à aucune conclusion au sujet de l'excrétion de l'or par l'urine à la suite du traitement par le BAL.

L'auteur formule des recommandations sur la posologie, en partie d'après les publications antérieures sur le sujet, et en partie d'après l'expérience limitée acquise avec la série de cas présentée ici. Il fait une distinction entre l'emploi du BAL pour le traitement des intolérances graves et celui des intolérances légères.

# ON THE OCCURRENCE OF NEUROPATHIC ARTHROPATHIES IN PERNICIOUS ANAEMIA

BY

PENTTI I. HALONEN and KLAUS A. J. JÄRVINEN

*From the Third Medical Clinic of the University of Helsinki\* and from the Hospital of the Wihuri Research Institute*

Among the admissions to our clinic there was a case of severe anaemia perniciosa myelosis (subacute combined degeneration of the spinal cord) associated with painless joint disease. The tendon reflexes of the lower limbs were lost, there was considerable decrease in pain sensibility and deep sensibility, and the gait was markedly ataxic. The x-ray findings revealed alterations in the joints, and particularly in the knee bone a close resemblance to neuropathic joint changes. These alterations suggested to the radiologist that tabes dorsalis might be present in this case. Since the possibility of tabes was excluded by thorough examination, the suspicion arose that the patient's joint changes, which so closely resembled neuropathic ones, might be attributed to myelosis funicularis.

As we have not been able to find in the literature descriptions of joint deformation associated with anaemia perniciosa myelosis, we consider a presentation of our investigation of this problem to be justified.

## Discussion on Anaemia Perniciosa Myelosis

It is known that pernicious anaemia often presents degenerative changes in the spinal cord, which condition is called myelosis funicularis. Data yielded by detailed histological examination and presented in various textbooks give evidence of patho-anatomical alterations in the spinal cord in up to 90 per cent. of cases of pernicious anaemia. Clinical evidence of myelosis is markedly less frequent, being present, according to various authors, in from 8 to 30 per cent. With regard to their location and histological picture, these changes—which may be very pronounced—bear resemblance to tabetic changes in the spinal cord. Also the clinical picture of pernicious myelosis is similar to

that of tabes. The literature actually points out the tabetiform manifestations of pernicious myelosis. The fact being that the spinal alterations in pernicious myelosis and the clinical picture of this condition bears such close resemblance to the corresponding changes and signs in tabes, it seems reasonable to assume that pernicious myelosis also might present changes in the joints similar to those in tabes. This belief is given additional support by the observation that the lesion of the spinal cord does not seem to be of necessity a strictly specific one in order to produce a neuropathic joint lesion. The literature describes cases in which spinal changes, due to a variety of causes, are responsible for this type of joint lesion: for example, traumatic or subacute myelitis, trauma from tumour, or constant compression of the spinal cord resulting from tuberculous spondylitis. It has been found that even a peripheral nerve lesion or cerebral paralysis has led to such a joint lesion (Pribram, 1902). Neurogenic arthropathy has also been found associated with diabetic neuropathy (Forster and Bassett, 1948). In addition to tabes, we may possibly mention syringomyelia as the best known of all the agents of neuropathic arthropathies.

## Material of the Present Investigation

Our material consists of fifty-two established cases of pernicious anaemia. Most of these patients have received repeated hospital care. Clinical symptoms of myelosis were present in twelve. All syphilitic patients have been excluded from the material by careful histories and by repeated blood analysis, as well as by liquor tests in cases of myelosis. All patients were subjected to systematic x-ray examinations of the knee and hip joints. The distribution of our material and the revealed joint changes are shown in Tables 1 and 2.

\* Director, Professor Östen Holsti, M.D.



TABLE 1

## CASES OF PERNICIOUS ANAEMIA WITH NO SIGNS OF MYELOSIS FUNICULARIS

Age	Sex	Duration of pernicious anaemia in years	X-ray changes in joints *	
			Hips	Knees
78	F	3	0	0
77	F	9	+	+
77	F	9	+	0
76	F	7	0	+
76	F	2	0	++
75	F	3	0	0
73	M	7	+	0
72	F	5	0	0
71	F	20	0	0
71	F	2	0	0
71	F	8	0	+
71	F	6	+	+
70	M	20	0	0
69	F	3	0	0
69	F	2	0	0
68	M	1	+	0
68	F	9	+	+
68	M	20	0	0
67	F	12	0	0
66	F	2	0	+
66	F	9	0	0
66	F	20	0	+
66	M	3	0	+
65	M	1	0	+
65	F	7	0	0
64	F	2	+	0
63	F	5	+	0
63	F	1	0	0
63	F	8	0	0
59	F	2	0	0
57	M	14	0	+
57	F	8	0	0
55	M	1	0	0
55	M	3	0	+
53	M	11	0	0
51	F	3	0	0
50	F	5	+	++
45	F	2	0	0
41	M	6	0	0
36	F	9	0	+

\* The joint changes have been assessed as follows:

- 0 No pathological changes in the joints.
- + Changes considered to be manifestations of mild osteo-arthritis.
- ++ Marked changes of osteo-arthritis.
- +++ Excessive joint changes. Severe manifestations of osteo-arthritis with additional presence of loose fragments in the vicinity of the articular surfaces. The interarticular space is, as a rule, markedly narrowed or entirely lost. There may be a tendency toward subluxation of the joints.

We have attempted to make the classification of the x-ray findings showing the various degrees of alteration as objective as possible by letting the radiologist carry out the grouping only on the basis of the radiographs presented to him, without any information whatever about the clinical examinations.

## Discussion of our Findings

As will be seen from the two Tables, it is in cases of myelosis funicularis that joint changes most frequently occur, and indeed all the most serious changes in the knee joint fall into the group of severe myelosis. Quite naturally our patients, most of whom were old people (the average age of those without myelosis being 64 years, those with mild myelosis 63, and those with severe myelosis 66 years) also presented changes in the joints attributable to other causes, particularly to simple osteo-arthritis of old age. The frequency of the joint changes and the severity of the alterations in the knee joints being appreciably greater in the group with myelosis than in those with other types of pernicious anaemia (according to the control material), we find it reasonable to assume that the condition of myelosis funicularis and the presence of joint changes bear a causal relation to each other. For the reasons offered above the theory of a neuropathic aetiology for these changes seems justified. This view is supported by the frequency of joint changes in pernicious myelosis, by their scarcity in other types of pernicious anaemia, and particularly by the x-ray picture of the extreme changes concerned, which is similar to those of other known cases of neuropathic arthropathies: severe changes of osteo-arthritic type, the appearance of osteophytes, marked narrowing of the inter-articular space, loose fragments found in the vicinity of the joint surfaces, and a tendency to develop subluxation (Figs. 1 and 2). We do not consider that the fact that the joint changes described do not appear in every single instance of myelosis contradicts our view (in two serious cases of myelosis there were no recognizable changes in the joints). Tabes and syringomyelia, for instance, as far as we know, present simultaneous severe neuropathic joint changes relatively seldom.\*

A view generally held, and confirmed particularly by animal tests (Katsuki, 1936), is actually that a lesion of the nerve fibres alone cannot be responsible for neuropathic arthropathies. Additional agents, such as local trauma, metabolic disorder, etc., are needed to produce them. We think it has not been possible to carry out an analysis of such additional factors on account of the scanty material available.

The clinical picture of extensive joint changes appearing in the knees in the more severe instances of myelosis is one of marked thickening of the knee joints and, on flexion, crepitation louder than usual.

More pronounced motor disturbances have not been encountered. In one of the cases of this group occasional locking of the knee joints occurred

TABLE 2

## CASES OF PERNICIOUS ANAEMIA WITH SIGNS OF MYELOSIS FUNICULARIS

	Age	Sex	Duration of pernicious anaemia in years	Duration of the signs of myelosis funicularis in years	Radiographic changes in joints	
					Hips	Knees
Group A	71	F	8	2	0	0
	70	M	1	1	++	+
	68	M	6	>2	+	+
	61	F	13	>1	++	+
	43	F	19	7	+	0
Group B	71	F	>1	>1	+	++++
	69	F	17	>2	+	++++
	67	F	23	2	+	+
	66	F	10	>5	+	++++
	64	M	>3	>3	++	++++
	64	F	10	>1	+	++++
	62	F	>1	>1	0	0

Group A.—Slight cases of myelosis funicularis with distinct reflex disturbances. As a rule, a marked uncertainty or loss of tendon reflexes in the lower extremities, and a distinct decrease of pain and deep sensibility. Walking fairly normal.

Group B.—The more serious forms of myelosis funicularis. Tendon reflexes of the lower extremities completely lacking. Walking distinctly ataxic. Pain and deep sensibility markedly decreased.

very late in the patient's history. Alterations in the hip joints in the presence of myelosis have, as a rule, produced no manifest clinical symptoms. No painful joints have been seen in the presence of arthropathies associated with pernicious myelosis and this is true of neuropathic joint lesions in general. It is the absence of pain symptoms that presumably explains the fact that, as far as we know, no attention has formerly been paid to these marked alterations in the joints.

Since, according to what has been said above, it seems reasonable to believe that neuropathic changes in the joints may develop pernicious anaemia associated with myelosis funicularis, we think it more justified than ever before to call attention to the prevention and treatment of myelosis funicularis.

#### Summary

Our investigations comprised fifty-two cases of pernicious anaemia, five of which showed mild myelosis funicularis and seven a severe type of the disease. Joint changes, particularly in the knees, were seen in the presence of myelosis, and the most extensive changes were found in the cases of severe myelosis. In two cases, however, no—or only slight—joint changes were seen. In cases without myelosis there were comparatively few and only mild joint lesions. In the opinion of the writers the

joint changes detected are both clinically and radiologically of the type of neuropathic arthropathies.

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#### Sur la Fréquence des Arthropathies Nerveuses dans l'Anémie Pernicieuse

##### RÉSUMÉ

Nos recherches ont porté sur cinquante-deux cas d'anémie perniciieuse dont cinq présentaient une légère sclérose systématisée et sept une forme plus grave de la maladie. On a observé des lésions articulaires, particulièrement dans les genoux, chez les malades atteints de sclérose médullaire, et ce sont les sujets les plus gravement atteints qui présentaient les lésions les plus étendues. Deux malades ne présentaient cependant que des lésions articulaires très légères ou pas de lésions. Les autres cas d'anémie perniciieuse ne présentaient que des lésions articulaires relativement peu nombreuses et peu marquées. Les auteurs considèrent que les lésions articulaires observées appartiennent cliniquement et radiologiquement à la catégorie des arthropathies nerveuses.

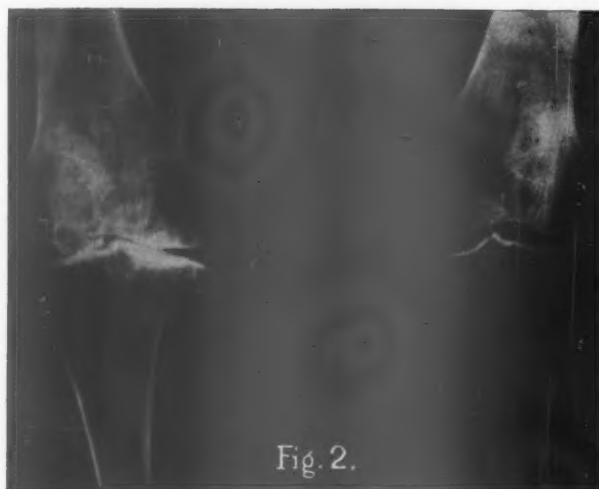


FIG. 1 and 2.—Radiographs of a patient, aged 66, who has been suffering from anaemia perniciosa for ten years and has had a strong myelosis funicularis for the last five years. There are severe changes of osteoarthritic type, especially in the right knee. Note also the appearance of osteophytes, marked narrowing at the interarticular spaces, and loose fragments in the vicinity of joint surfaces.



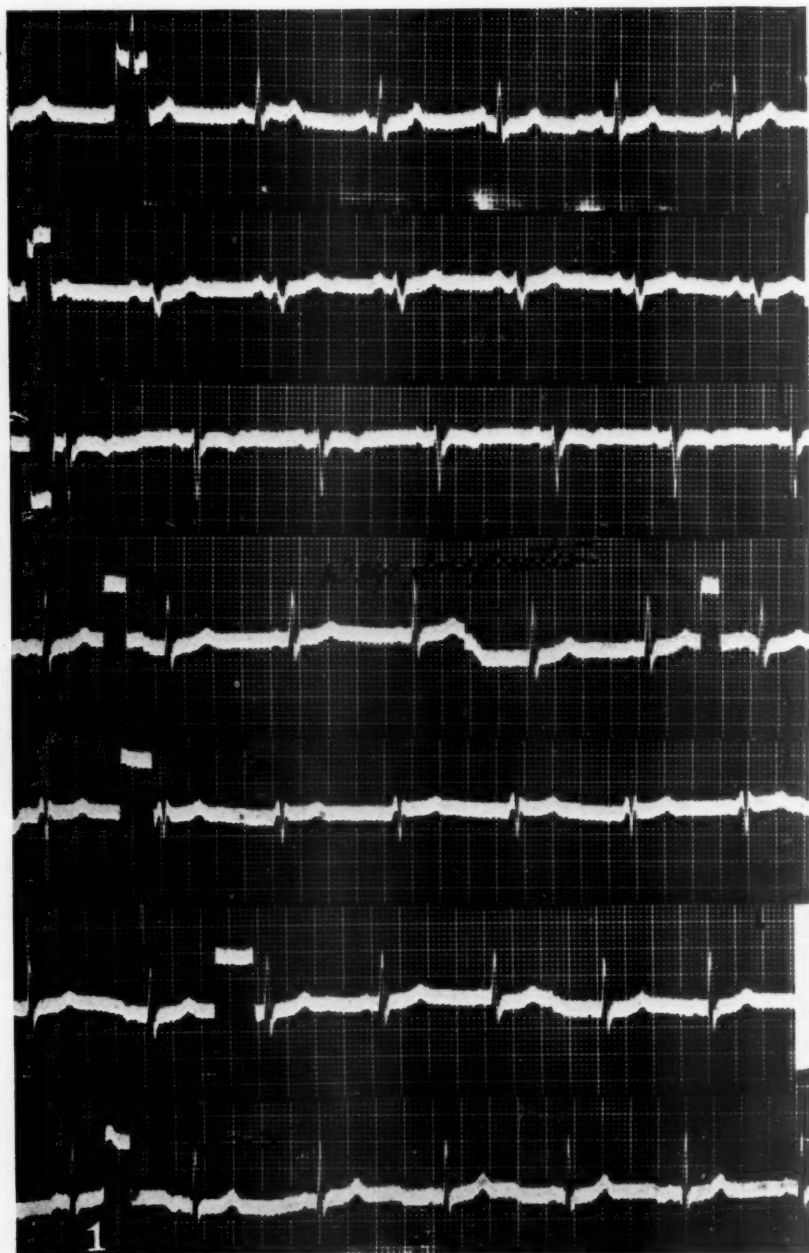


FIG. 1.—Electrocardiogram taken on July 3, 1947, showing left axis shift and a QRS duration of 0.11 second in lead II, but considered normal.

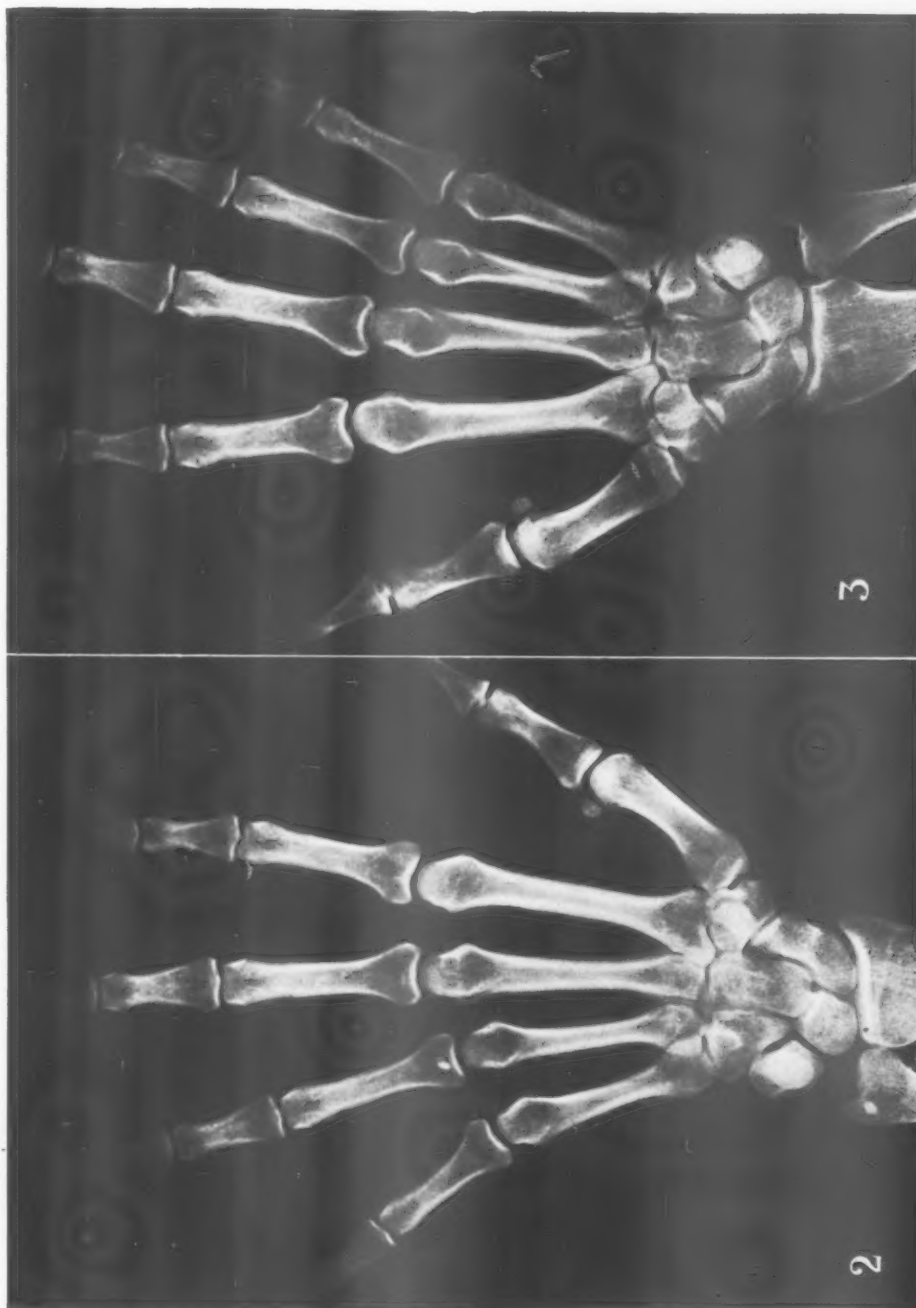


FIG. 2.—Radiograph of the left wrist and hand taken on June 25, 1947, showing no bone or soft-tissue abnormality.

FIG. 3.—Radiograph taken at the same time of the right wrist and hand showing no bone or soft-tissue abnormality.



FIG. 4.—Radiograph of the left shoulder taken on June 25, 1947, showing no bone or soft-tissue abnormality.



FIG. 5.—Radiograph of the right shoulder showing no bone or soft-tissue abnormality.

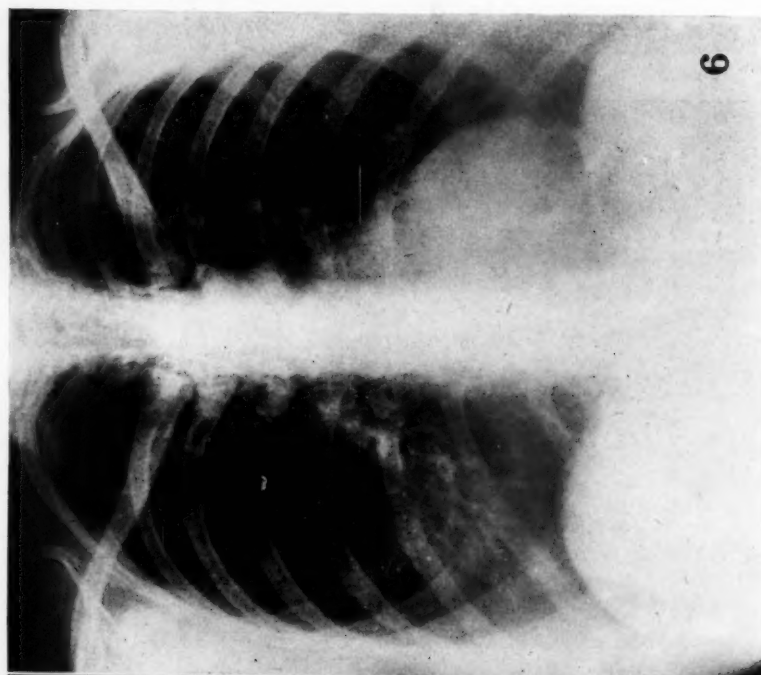


FIG. 6.—Radiograph of the chest taken on June 24, 1947, showing no pulmonary or cardiac abnormality.



## PALINDROMIC RHEUMATISM\*

BY

SAMUEL A. WOLFSON and MARVIN S. ALTER

*Wadsworth General Hospital, Veterans Administration, Los Angeles, California*

In 1941 and 1944 Hench and Rosenberg reported their observations on an hitherto undescribed recurrent, afebrile form of joint disease to which they applied the term "palindromic rheumatism". "Palindromic" means "recurrent" or "subsiding without coming to a head" and is descriptive of the many sudden and rapidly subsiding attacks which characterize the condition. The most remarkable feature of this rather rare disease is that the affected joints escape anatomical injury in spite of scores or even hundreds of attacks. These authors furnished the criteria by which this disease could be differentiated from other arthropathic disorders, and in particular from rheumatoid arthritis both in its well known and its "episodic" forms. A number of subsequent observers have reported additional cases which conform to the original descriptions. The aetiology remains obscure.

Because of the benign prognosis it is essential that such cases be recognized and so classified. It is hoped that a report of an additional case and a review of the literature will stimulate further observations and bring into relief factors which may help to explain the disease.

### Case Report

A white woman, 42 years of age, was admitted to hospital on June 20, 1947, with complaints of pain, redness, and swelling of the wrist, shoulders, and finger joints. She was a multigrapher and stenographer. The past history revealed only an "allergy to milk", manifested by "blotches on the hips and elsewhere", which disappeared while she was in military service but reappeared following separation from the Service. Social, family, and menstrual histories and routine psychiatric survey were non-contributory. A review of the systems was negative other than for the presenting complaints. She had been in the Service from August 28, 1943, until April 30, 1946, and had not been overseas.

While in the Service the patient's duties, which involved

frequent lifting of heavy supplies, had to be modified because of pains in the back. She was assigned to a multigraphing machine, the operation of which required striking the ball of a lever-arm with the palm of the hand. Soon after this, in June, 1944, she experienced the first definite attack of pain, redness, and swelling of joints of the right middle and ring fingers. Shortly thereafter both shoulders became red, swollen, and painful. There then elapsed a period of almost three years during which time no attacks occurred.

Before entry to hospital she had been doing stenographic work after many months of no such occupation. In April, 1947, the left shoulder became stiff and painful without redness or swelling. This subsided in a few hours. In May, 1947, a metacarpophalangeal joint developed pain and swelling. This also subsided in about twelve hours. There then followed approximately five attacks of pain, redness, and swelling involving the hands, wrists, and shoulders over a period of one month. No two joints were involved simultaneously. Some relief was obtained from heat and the use of salicylates.

On June 14, 1947, the right shoulder became red, swollen, and painful. The patient consulted the school physician, who suspected an early rheumatoid arthritis and advised hospitalization for observation. She was hospitalized on June 20, 1947, by which time all signs of the attack had disappeared. Thus, there had been approximately eight attacks in two months, subsiding promptly and leaving no residuals. At no time had there been any loss in weight or other constitutional symptoms.

The patient was well developed, well nourished, and moderately obese. The conjunctivae were clear. The pupils were equal, regular, and reacted to light and accommodation. The ocular fundi were normal. The nose was normal. The teeth were in good repair. Small tonsillar tabs were present on both sides but were not infected. The ears were normal. The thyroid was not enlarged and there were no nodules. The trachea was in the midline. The breasts were normal. The lungs were normal. The heart was not enlarged and the rhythm was regular. The first sound at the apex and the second sound at the pulmonic area were split; P 2 was slightly louder than A 2 and there were no murmurs. The blood pressure was 110 systolic and 70 diastolic. The liver and spleen were not palpable. Pelvic and rectal examinations were negative. There were no

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hernias or adenopathy. Neurological examination was normal. The peripheral vascular system was normal. The skin was normal in colour and texture.

The erythrocyte count was 4,760,000 per c.mm. of blood and hemoglobin 94 per cent. The leucocyte count was 8,300 per c.mm., with 72 per cent. neutrophils and 28 per cent. lymphocytes. The bleeding time was 3 minutes and clotting time 7 minutes. The blood uric acid was 3.6 mg. per 100 c.cm. and blood cholesterol 243 mg. per 100 c.cm. with 191 mg. per 100 c.cm. esters (normal for cholesterol in this laboratory is 240 to 360 mg. per 100 c.cm.). Blood iodine level was 5.3 mg. per 100 c.cm. Urinalysis was normal and blood serology negative. Basal metabolic rates on two determinations were respectively plus 12 and minus 4. Agglutination test for *Brucella* was negative. The sedimentation rate was 23 mm. in 1 hour (Cutler—normal up to 10 mm. in 1 hour); subsequent determinations made between and during attacks were respectively 4 mm. and 22 mm. in 1 hour. The electrocardiogram showed a QRS time of 0.11 second in lead II and a left axis shift with a negative deflection in lead III which became positive on deep inspiration (Fig. 1).

Radiographs of the hands, wrists, shoulders, dorso-lumbosacral spine, and pelvis showed no evidence of arthritis or soft tissue changes (Fig. 2, 3, 4, and 5). A chest film showed no pulmonary or cardiac abnormality (Fig. 6). (For illustrations see pp. 156-8.)

Skin tests for food allergy were positive for lamb, clams, codfish, shrimp, rice, and wheat. The allergist attached no significance to these tests, and no relationship was observed between the ingestion of some of the foods and the attacks of arthritis.

The temperature and pulse remained normal. The highest recorded temperature was 99° F. on two occasions.

During hospitalization the patient had at least twelve episodes of pain and stiffness of the fingers, wrists, and shoulders, without redness or swelling. On approximately six occasions she had attacks of pain with redness and swelling which were observed by hospital personnel and other patients but which were not recorded. Attacks were specifically recorded on the following dates.

*June 23, 1947.*—There was pain, redness, and swelling of the proximal interphalangeal joint of the left middle finger. The swelling involved the articular, peri-articular and para-articular tissues with small, interspersed areas of normal colour in the para-articular area. The joint was tender and stiff. The attack subsided in twelve hours without residuals.

*June 24, 1947.*—The patient was awakened at 1.30 a.m. by pain in both shoulders. No redness or swelling was noted. Sedimentation rate was 23 mm. in 1 hour. The pain entirely subsided during the day.

*June 26, 1947.*—There was pain, redness, swelling, and stiffness of the proximal interphalangeal joint of the left index finger, but marked improvement three hours later and complete subsidence in twelve hours. The sedimentation rate taken the following day was 4 mm. in 1 hour.

*July 14, 1947.*—There was pain, redness, and swelling of the metacarpophalangeal joint of the right index

finger, with articular, peri-articular, but no para-articular involvement.

*July 16, 1947.*—There was swelling, pain, and tenderness without redness of the left wrist.

Pyribenzamine was prescribed in doses of 50 mg. four times daily to observe the effect on a possible allergic factor. However, at least three additional attacks were observed during the therapy.

The estimated number of attacks from April to July was thirty-four, of which nine were observed in a period of one month. They followed a consistent pattern and had no relationship to work or weather under our observation. The onset was very rapid and always occurred during the night. Both shoulders were painful on two occasions, and two fingers were red, swollen, and painful on one occasion, but the rest of the attacks were monoarticular. The height of the attack was reached in from one to two hours, at which time the pain was severe, aching in character, and intensified by slight motion. Improvement began as promptly as three hours after the onset, with the majority of attacks subsiding within twelve hours and none lasting longer than twenty-four. The condition always regressed completely and left no subjective or objective residuals. No subcutaneous nodules or involvement of finger pads were observed at any time.

In spite of the number and severity of attacks the patient remained in excellent health and frame of mind. A diagnosis of palindromic rheumatism was made. The patient was assured of an excellent prognosis, advised on the symptomatic relief of the attacks, and discharged from the hospital on July 24, 1947, after thirty-five days of hospitalization.

### Discussion

In their original description of palindromic rheumatism Hench and Rosenberg (1941, 1944) enumerated the following as the principal features of the disease: multiple attacks of pain, redness, and swelling of one or more joints, rapid to sudden in onset, of varying intensity, lasting hours to days, subsiding spontaneously, not attended by constitutional reactions, and showing articular exudation only in occasional instances; absence of abnormality in radiographic and laboratory examinations, and absence of functional and morphologic residues in spite of dozens or even hundreds of attacks over a period of years.

The only available pathological observations were made by Hench and Rosenberg. The changes which they observed consisted of acute inflammation of the synovial membrane and capsule of the joint with the presence of large numbers of polymorphonuclear leucocytes. In some instances the joint cavity contained a fibrino-purulent exudate, and tendon sheaths were sometimes involved in the inflammatory process. All tissues returned to normal after the attack, and cultures of the fluid from the joint and tendovaginal spaces remained

sterile. Hench and Rosenberg differentiated the disease from the angioneural arthroses of Solis-Cohen (1911) and the allergic rheumatism of Kahlmeter (1939).

Since the original report of thirty-four cases there have been only eighteen cases added to the literature. Four were reported in England (Parkes Weber, 1946; Wingfield, 1945; Neligan, 1946), one in France (Forestier, 1946), and thirteen in the U.S.A. (Thompson, 1942; Mazer, 1942; Ferry, 1943; Paul and Logan, 1944; Grego and Harkins, 1944; Cain, 1944; Paul and Carr, 1945; Salomon, 1946; Hopkins and Richmond, 1947). The present case brings the total to fifty-three.

The incidence of the disease as seen at the Mayo Clinic (Hench and Rosenberg, 1944) is approximately one-tenth of 1 per cent. of all cases of articular and muscular diseases. Bach (1947) gives the latest available figures for the incidence of rheumatism and arthritis in the U.S.A., based on the National Health Survey made by the United States Public Health Service in 1937. There were 6,850,000 cases of "rheumatism" yearly. Analysis of the survey disclosed that "arthritis" was the single largest group and attacked 3,000,000 persons, mostly adults, annually. Thus, using one-tenth of 1 per cent. as the estimated incidence, it is likely that there exist 3,000 cases of palindromic rheumatism yearly. It is highly probable that a number of cases are seen at various arthritic centres and additional reports may be anticipated in the future.

The sex ratio in the Mayo Clinic series was 15 males to 19 females. In the subsequent reports there were 12 males and 6 females. Thus, the total reported incidence is 27 males to 25 females. Inclusion of the authors' case brings the number for females to 26. As has been pointed out by Hench and Rosenberg and others the incidence in rheumatoid arthritis is predominantly female and in gouty arthritis predominantly male.

In the Mayo Clinic series the age of the patients varied from 21 to 73 years (average 42 years), the onset of the disease having occurred between the ages of 13 and 68 (average 34.9 years). In the subsequently reported cases the age varied from 4 to 53 years (average 33.1 years),\* the onset of the disease having occurred between the ages of 4 and 49 (average 23.5 years). The difference in average ages between the two groups is appreciable. This is in great part accounted for by Salomon's four patients who were 4, 6, 9, and 10 years old, respectively. The proper inclusion of these cases is doubtful inasmuch as all attacks subsided permanently within a few weeks. When these are omitted from

the group of subsequently reported cases the average age becomes 41 years and the average age at onset of the disease becomes 29.2 years, and these figures differ very little from those of the Mayo Clinic.

The frequency and duration of the attacks, the number of joints involved, and the length of intervals between attacks in the cases reported differed in no way from the original observations by Hench. The reported frequency varied from two or three attacks a day to one in two months. Monarticular attacks involving a different joint at different times predominated over polyarticular attacks, and the joints most often involved were those of the wrists and hands. The arthritis developed rapidly to suddenly, varied in intensity from mild to severe, and lasted from one hour to two weeks.

Redness was reported in twenty-nine cases (88.5 per cent.) of the original series and in twelve (66.6 per cent.) of the later reports. Swelling occurred in all thirty-four (100 per cent.) of the Mayo cases and in seventeen (94.4 per cent.) of the subsequent cases. Subcutaneous nodules were reported in three of Hench's cases and in the only case in the subsequently reported series in which joint swelling was absent (Parkes Weber's Case 1). The authors' patient presented no nodules. More recently Hench (1948) reported occasional heat and swelling of the finger pads. Swelling in or about the joint is the most consistent objective finding.

Pain was present in all of Hench's patients and in sixteen of the subsequently reported eighteen cases. Grego and Harkins (1944) reported itching and white swelling in their case, which makes the diagnosis of palindromic rheumatism a little uncertain.

In Hench and Rosenberg's series all the patients were afebrile, but in later observations Hench noted that febrile attacks do occur, with elevations of temperature to 100° F. for a few hours to a day or two, but that such occurrences are rare (see Hopkins and Richmond, 1947; also Hench, personal communication). Fever was present in only one of the subsequently reported cases (Grego and Harkins, 1944), but Hench (1948) believes that this case may represent an early, atypical, episodic rheumatoid arthritis because of the marked anaemia, loss of weight, protracted symptoms, and frequency of polyarticular attacks.

In Hench's series there was no anaemia or leucocytosis; the differential count frequently showed a relative lymphocytosis but no eosinophilia. The sedimentation rate was generally found to be slightly elevated during but not between attacks. In reports by subsequent observers a reduction of haemoglobin was noted in three cases, a diminished erythrocyte count in four, leucocytosis in two, and

\* Wingfield failed to report the patient's age; and Weber recorded the current ages but not the ages at the onset of the disease.



eosinophilia in none. Sedimentation rates were found to be normal or mildly accelerated. Hench found the blood uric acid, calcium, phosphorus, and phosphatase normal. Blood uric acid determinations performed by other observers in ten cases and blood cholesterol tests in two cases were all within normal limits. Hench reported a moderate elevation of fatty acids and total lipoids, but the significance of these findings has not as yet been determined. Brucella agglutination tests were done in three cases (Wingfield, 1945; Cain, 1944; Hopkins and Richmond, 1947) and were negative. A Brucella skin test performed in a single case (Paul and Logan, 1944) was also negative. Hench and Rosenberg as well as subsequent observers found radiographs of the joints to be consistently negative regardless of the number of attacks suffered by the patients.

No electrocardiographic studies were reported by Hench. Tracings were mentioned in only six of the subsequent cases (Wingfield, 1945; Paul and Logan, 1944; Grego and Harkins, 1944; Cain, 1944; Salomon, 1946; Hopkins and Richmond, 1947), and were reported as normal. In the authors' case the QRS interval was 0.11 second, but this finding is considered to be without significance. Allergy could not be proven as an aetiological factor at the Mayo Clinic. Skin tests in the author's case were positive for certain foods, but the results were not considered significant and attacks were not provoked by some of these foods ingested while the patient was under observation. Parkes Weber's (1946) Case 1 had episodes of Menière's syndrome and attacks of iritis in addition to the joint pains, but no two of these groups of symptoms developed concurrently. Parkes Weber believed that all three manifestations were allergic in origin and that the joint pains probably represented palindromic rheumatism in a mild form. In his second case he pointed out that there were subcutaneous nodules present but no pain or redness of the joints, and considered the condition to be midway between angioneurotic oedema and palindromic rheumatism. In a discussion of twenty-seven cases of recurrent allergic arthritis Vaughan (cited by Hench, 1948) stated that in ten there was a fairly close resemblance to palindromic rheumatism and that allergens might be a principal cause of the latter. Hench, commenting on Vaughan's conclusion, stated that the individual cases were not fully described and that data sufficient for an independent appraisal were lacking.

In none of the cases of the Mayo Clinic series, nor in subsequent reports of cases, were foci of infection believed to be related to the attacks.

Hench found only questionable relationship of trauma and work to the attacks. In only four of

his cases did slight trauma appear to provoke attacks, and in two cases the attacks were occasionally related to overwork. Trauma was discussed in relation to aetiology by Hopkins and Richmond (1947), Mazer (1942), and Paul and Logan (1944); and the authors' case presents a strong indictment of work and trauma except for the initiation of the attacks during the patient's stay in the hospital.

Psychogenic factors were apparently related to attacks in only one case in the Mayo series. In the subsequent reports six of eighteen patients appeared to have some psychogenic basis for their attacks. Mazer's patient became attack-free during one period and had diminished intensity and lessened frequency of attacks during another period after making spiritual and economic adjustments on both occasions. Ferry (1943) believed that there was a definite premenstrual timing in some of his patient's attacks and that the majority of attacks occurred under the stress of worry and emotional strain. This same patient was found to have a functional colitis and occasional tinnitus, vertigo, and nausea before the menses. She showed no reaction to skin tests with allergens.

Paul and Logan observed that their patient's attacks were associated with mild nausea and often followed episodes of anger and nervousness. Cain's patient had a definite tendency to worry, was irritable, and suffered from mild insomnia. Neligan reported that his patient's attacks began after months of great war strain and anxiety over a son who had disappeared in Malaya. Paul and Carr suggested that psychogenic factors may be involved. These observations are too few and too superficial to attach great significance to them. The progress in psychosomatic medicine in recent years has focused attention on the numerous physical manifestations of psychic disability, but much more detailed study will be necessary before a psychogenic basis can be accepted for the causation of palindromic rheumatism.

Hench (1947, 1948) stresses the importance of distinguishing palindromic rheumatism from episodic, atypical rheumatoid arthritis, in both of which there are evanescent attacks and appreciable intervals of freedom from symptoms. Ropes and Bauer (1945) believe that the former is actually a form of atypical rheumatoid arthritis, but Hench considers that the two conditions are unrelated and that they can readily be differentiated. He points out that in palindromic rheumatism the attacks are usually of very short duration, involve widely scattered joints, affect the finger pads at times, frequently include para-arthritis, and are not accompanied by constitutional reactions. On the other hand, episodic rheumatoid arthritis tends to recur in

"favoured" joints, shows higher sedimentation rates during seizures and often persistently elevated rates between seizures, and frequently attacks some particular joint which is thereafter never entirely free from involvement and which ultimately becomes the seat of chronic disease. Moreover, articular biopsies in the episodic cases may reveal changes which are characteristic of rheumatoid arthritis. Inasmuch as there is no evidence that the two conditions have a common aetiology, and inasmuch as Hench's extensive and careful observations have provided a valid basis for clinical differentiation, it is advisable to accept the concept of separate entities. It would indeed be difficult to regard a condition in which joints may survive hundreds of attacks without residual damage as identical with a disease in which a large number of attacks invariably leads to permanent and manifest injury.

#### Summary and Conclusions

A detailed report of a case of palindromic rheumatism is presented. The original cases of Hench and Rosenberg are reviewed and compared with those of subsequent observers. The clinical, laboratory, radiographic, and pathological-anatomical features are reviewed. The possible significance of work, trauma, and psychogenic influences in relation to aetiology are discussed, but definite conclusions must await future investigations. Utmost care should be taken to distinguish between palindromic rheumatism and the episodic form of rheumatoid arthritis, conditions which, under present knowledge, should be considered as separate entities.

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 (See also abstracts, p. 191 of this issue.)

#### Rhumatisme Palindromique

##### RÉSUMÉ ET CONCLUSIONS

Les auteurs présentent une observation détaillée d'un cas de rhumatisme palindromique. Ils analysent les observations originales de Hench et Rosenberg et les comparent aux observations ultérieures. Ils passent en revue les caractères cliniques, biologiques, radiographiques, et anatomo-pathologiques. Ils discutent la signification étiologique possible de l'effort, du traumatisme, et des influences psychogènes, mais considèrent qu'il est indispensable de pousser plus avant les recherches avant de pouvoir formuler des conclusions définitives. Il est nécessaire d'établir une distinction très nette entre le rhumatisme palindromique et la forme épisodique de l'arthrite rhumatismale qui, dans l'état actuel des connaissances, doivent être considérées comme tout-à-fait distinctes.

# THE GROSS ANATOMY OF THE PERI-ARTICULAR TISSUES OF THE SHOULDER JOINT

BY

W. J. H. NAUTA and J. M. F. LANDSMEER

*Department of Anatomy and Embryology, State University, Leiden, Netherlands*

Since it has become evident that the pathological changes underlying disorders of the shoulder mechanism are not, in a number of cases, localized in one of the major joints of this region (scapulo-humeral and acromio-clavicular joints), but, instead, in the tissues surrounding these joints, the need for a thorough knowledge of the anatomy of this tissue has imposed itself on all those who have to deal with such disorders. In the current textbooks of anatomy, however, little attention has been paid to the structures surrounding the shoulder joints. Although more or less adequate accounts of the matter are found in Rouvière's (1945) and in Frohse and Fraenkel's (1908) textbooks, and in some special papers dealing with the subject (Henke, 1874; Pfuhl, 1934; Kahlmeter, 1941) the distribution of these works has, perhaps, not been sufficiently wide to provide for a satisfactory introduction of the pertinent facts into clinical medicine. It is for this reason that we submit the present account—which is based partly on the foregoing papers and partly on our own observations on a large amount of dissecting-room material—to those clinicians who will be most interested in the anatomical basis of shoulder movements.

## Anatomical Description

A glance at a suitable illustration in an atlas of anatomy will immediately disclose the important fact that the glenoid fossa of the scapula is overhung on the cranial side by an osteofibrous arch, the so-called fornix humeri, which is formed by (from before backwards) the coracoid process, the coraco-acromial ligament, and the acromion (Fig. 1a). The fornix humeri bridges the lateral exit of the supraspinous fossa (Fig. 4). The space between this arch and the glenoid fossa is largest dorsally, that is, under the acromion. A large part of this space is occupied by the tendon of the supraspinatus muscle (Fig. 1b).

The capsule of the shoulder joint is largely enveloped by the tendons of the muscles which surround the joint. The subscapularis, supraspinatus, infraspinatus, and teres minor tendons all join in the formation of what Poirier (1904) has aptly termed a musculo-tendinous cuff (coiffe musculo-tendineuse), surrounding and, to a variable extent, blending with the joint capsule. On the cranial side the cuff is completed by the coraco-humeral ligament, which bridges the gap between the supraspinatus and subscapularis tendons (Fig. 1b). Between the subscapular tendon and the coraco-humeral ligament there is a slit-like orifice (the oval foramen of Weitbrecht) which allows the bursa subscapularis to anastomose with the joint.

It is especially the cranial part of the musculo-tendinous cuff that demands our attention, since this part, which is formed by the supraspinatus tendon and the ventrally adjacent coraco-humeral ligament, is separated from the undersurface of the fornix humeri virtually only by space. During abductory movements in the shoulder joint the supraspinatus muscle withdraws its tendon through the narrow tunnel under the fornix humeri. At the final stage of the movement, however, the tendon is raised by its apophysis (the greater tubercle) to such an extent that its lateral part impinges on the acromion and the coraco-acromial ligament. Further abduction in the joint is checked by this occurrence, but it seems certain that some additional abduction is rendered possible by an outward rotation of the humerus, which moves the tendon and its apophysis backwards into a position underneath the acromion, where more space is available. In view of the ever-returning conflict between the upper part of the musculo-tendinous cuff on the one hand and the fornix humeri on the other, it is not surprising that a bursa has developed in the narrow space between the two. This bursa is usually designated the sub-deltoid bursa, but because this name is liable to



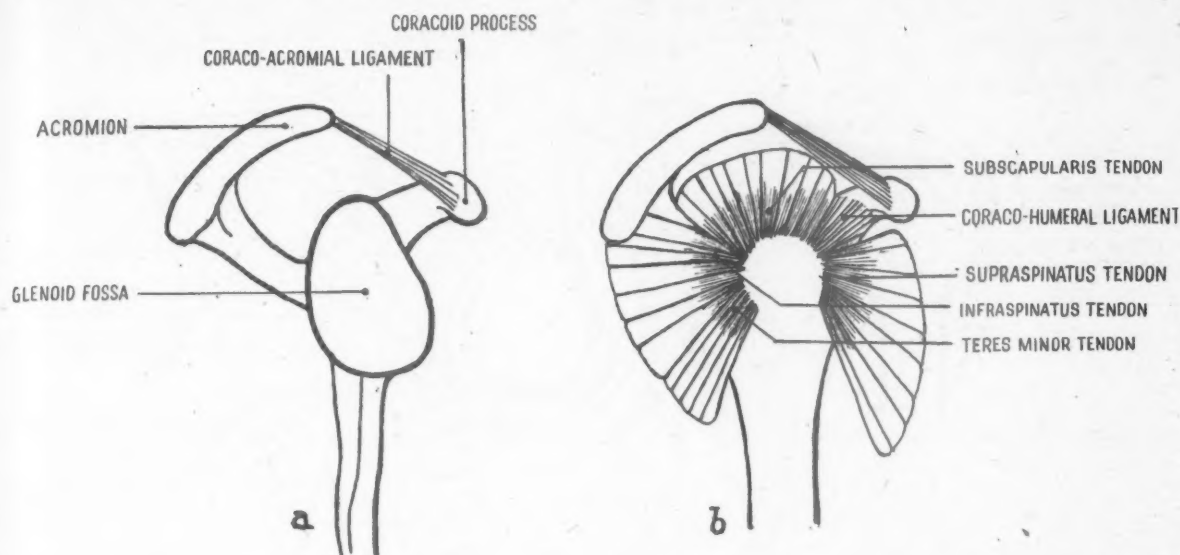


FIG. 1.—Schematic drawings of lateral aspects of: (a) fornix humeri, and (b) musculo-tendinous cuff of the shoulder joint. (b) has been redrawn and amplified from McGregor (1943).

cause confusion (see below) it will be referred to in the following as "subacromial bursa" (Fig. 3). To facilitate an understanding of its topography it will be necessary to deal with the fascial relations of the shoulder region.

**Fascial Relations of the Shoulder Region.**—On the medial side the coraco-acromial ligament (which covers the lateral exit of the supraspinous fossa) is continuous with the much thinner supraspinous fascia. Laterally, it continues into the important subdeltoid fascia, a connective-tissue sheet of considerable strength stretched out over the greater tubercle and the surgical neck of the humerus (Fig. 2, 4, 6). Dorsally, the subdeltoid fascia continues into the infraspinous fascia, a strong fascia covering the infraspinous and teres minor muscles, and ventrally it passes over into the subscapular fascia which covers the subscapularis muscle. The subdeltoid fascia can thus be regarded as the result of a junction of the several fasciae covering the muscles which take part in the formation of the musculo-tendinous cuff (that is, the fasciae subscapularis, supraspinata, and infraspinata). Distally, a small distance above the insertion of the deltoid muscle, the subdeltoid fascia blends with the periosteum of the surgical neck and is thus attached to the humerus.

**Subdeltoid Fascia.**—It will be clear from the foregoing description that the subdeltoid fascia is part of a vast sheet of connective tissue which envelops the whole complex formed by the upper part of the humerus, the shoulder joint, with its musculo-tendinous cuff, and the muscles contributing to this

cuff (Fig. 2). On the scapular side this sheet is divided into three divisions—the subscapular, supraspinous, and infraspinous fasciae—by the bony rims separating the scapular fossae of the same names; on the lateral surface of the upper part of the humerus the three divisions unite to form the subdeltoid fascia, which has a skeletal attachment to the surgical neck of the humerus. It will be noticed that the fornix humeri is a strongly reinforced strip of that part of the connective-tissue sheet under consideration which covers the superior part of the musculo-tendinous cuff (supraspinatus tendon and coraco-humeral ligament).

A further point of interest is the relation between the subdeltoid fascia and the short head of the biceps. The tendon of this muscle is sometimes found to possess a broad lateral-expansion blending with an aponeurotic subdeltoid fascia (Fig. 6). Although in the majority of cases this connexion is less strongly developed, a fibrous attachment of the lateral margin of the caput breve tendon to the subdeltoid fascia is a constant finding (Fig. 2b). It seems probable that the fascia can thus be made taut by the caput breve of the biceps.

On its ventral side the subdeltoid fascia is joined by the fascia coraco-clavi-pectoralis (costo-coracoid membrane). A superficial part of this fascia, after having covered the pectoralis minor muscle, extends laterally over the conjoined tendons of the caput breve of the biceps and the coraco-brachialis muscles and immediately afterwards comes to cover the subdeltoid fascia. After it has run freely over this fascia for a short distance the two fasciae blend

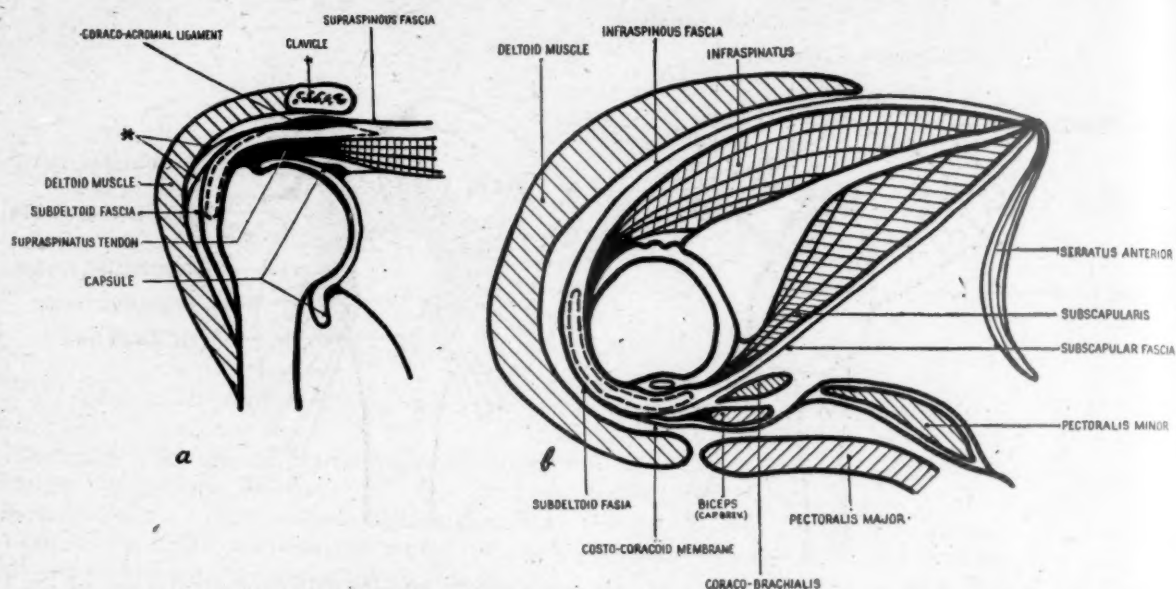


FIG. 2.—Schematic sections through the shoulder joint (a) in the frontal and (b) in the horizontal plane. The subacromial bursa is indicated by broken lines.

In (a) notice that the subdeltoid fascia is a lateral extension of the coraco-acromial ligament (the supraspinous fascia being the medial continuation of this ligament). Notice also that the coraco-acromial ligament and the supraspinatus tendon are incorporated in the wall of the bursa. The small bundles of the deltoid muscle attaching to the subdeltoid fascia are marked by an asterisk.

(b) shows the continuation of the subdeltoid fascia into the subscapular and infraspinous fasciae. Notice the relation of the subdeltoid fascia to the tendon of the caput breve m. bicipitis and to the costo-coracoid membrane (compare with Fig. 6).

along an approximately vertical line (Fig. 2b; in Fig. 6 the fascia has been rolled up to this line).

**The Subacromial Bursa.**—The subdeltoid fascia is covered by the deltoid muscle, with which it is connected by a loose, felt-like connective tissue. We have been unable to find a bursa in this tissue in any of our preparations. For this reason we have followed Frohse and Fraenkel (1908) in omitting the name subdeltoid bursa for what is more properly called the subacromial bursa. It is of importance to note that a rather variable number of small bundles of the deltoid muscle, originating from the tuberositas deltoidea of the humerus, is constantly found attached to the upper part of the subdeltoid fascia in a proximal direction (Fig. 2a). Presumably these bundles exert a distal pull on the fascia during abduction of the arm, and they may thus prevent the formation of folds in the fascia which would be liable to be incarcerated between the supraspinatus tendon and the fornix humeri.

Proximal to the distal attachment of the subdeltoid fascia to the periosteum of the humerus, a layer of extremely loose tissue is woven between the subdeltoid fascia and the surgical neck of the humerus. More proximally, just over the supraspinatus tendon, the subdeltoid fascia is separated

from this tendon by the subacromial bursa (see below). It may be inferred from this fact—and manipulation of the upper arm in the cadaver shows the inference to be correct—that every movement of the upper arm in the shoulder joint is accompanied by a displacement of the upper part of the humerus with the musculo-tendinous cuff against the inside of the fibrous sheath encapsulating these structures. Since the fornix humeri forms a rigid and fixed part of this sheath the displacement relative to the sheath is greatest at this point.

It is, therefore, not surprising that the subacromial bursa is constantly found to occupy the narrow space under the fornix humeri, separating the latter from the upper part of the musculo-tendinous cuff (the supraspinatus tendon and the coraco-humeral ligament). Friction, however, is exerted not only by the musculo-tendinous cuff but also by the outer surface of the greater tubercle, and it is exerted not only against the under surface of the fornix humeri but also against the inner side of the sub-deltoid fascia (the latter of these two points will be understood if one realizes that, as mentioned in the previous account, the subdeltoid fascia is kept extended during abduction by part of the bundles of the deltoid muscle (Fig. 2a)). This explains the

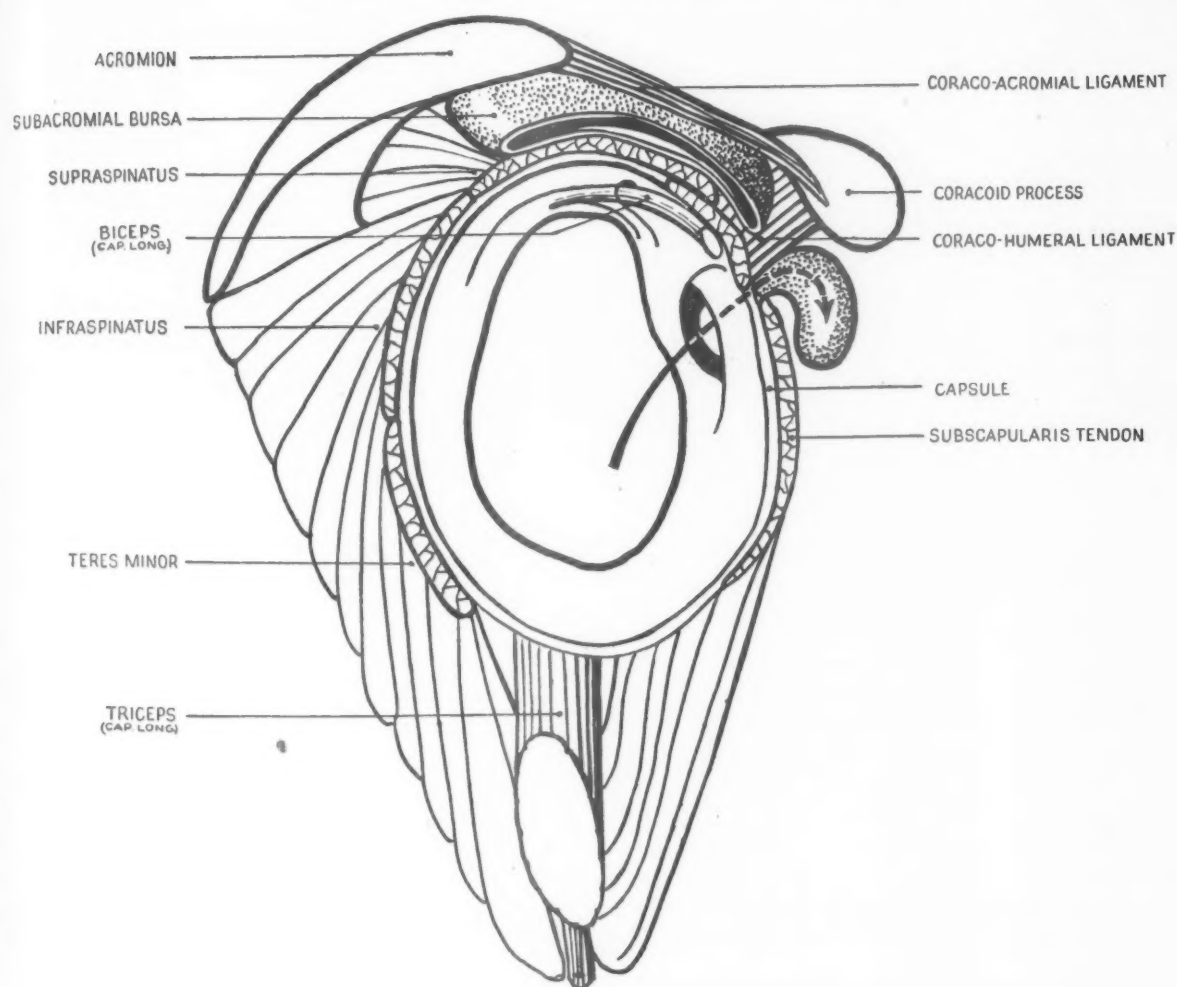


FIG. 3.—Semidiagrammatic drawing of the lateral aspect of the shoulder joint and its surroundings after exarticulation of the humerus. Notice that the capsule is in large part surrounded by the musculotendinous cuff, components of which are labelled. The coraco-humeral ligament radiates into the capsule. The subacromial bursa is situated between the upper part of the cuff and the fornix humeri. The subdeltoid fascia, which covers the bursa, has been removed. The arrow points through a foramen into the subcoracoid bursa.

fact that the bursa is constantly found to extend laterally beyond the insertion of the supraspinatus muscle over the outer surface of the greater tubercle and under cover of the subdeltoid fascia. Since this lateral extension necessarily follows the downward slope of the tuberosity, this is the deepest part of the subacromial bursa, and corpuscular substances are liable to collect here. The degree of lateral extension is, however, subject to important individual variation. A remarkably small lateral extension, for instance, is shown in Fig. 4; and Fig. 5 shows a subacromial bursa which reaches distally far over the lateral surface of the great tuberosity. When the arm is kept hanging down to the side of the body the opposite (medial or proximal) margin of the bursa rarely

extends for more than a small distance medially beyond the medial border of the coraco-acromial ligament. This small part of the bursa is covered by the supraspinous fascia (Fig. 2a). Dorsally, the bursa constantly extends for some distance underneath the acromion. To the ventral side the bursa does not, as a rule, extend farther than the base of the coracoid process, but Pfuhl (1934) whose paper gives a good impression of the variability of the bursa subacromialis, records several instances of larger ventral extension (recessus subcoracoideus) of the bursa.

With respect to the relation of the subacromial bursa to its surrounding tissues the following facts are of importance. As a rule, the bursa can easily



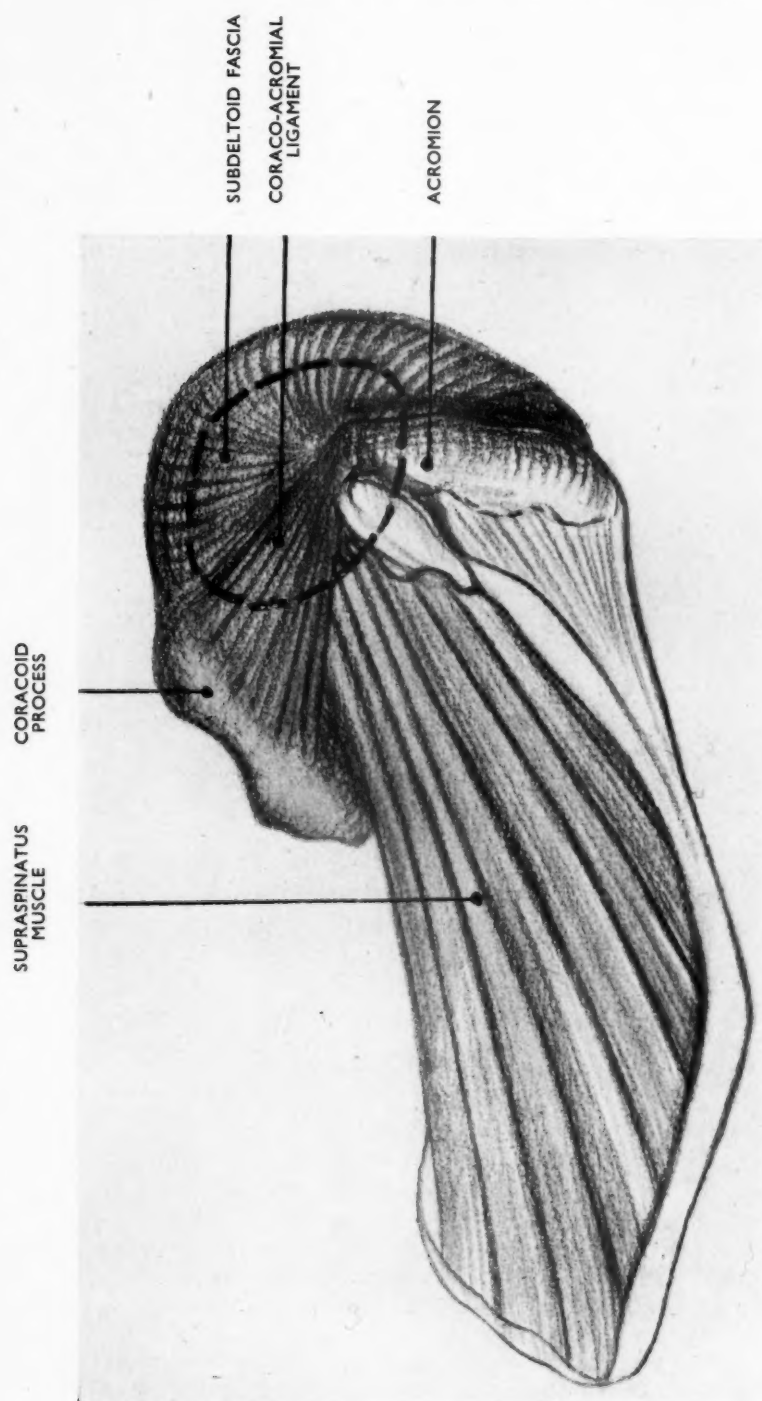


FIG. 4.—Cranial surface of the right shoulder after removal of the deltoid and trapezius muscles and the clavicle. Notice the continuity of the fornx humeri (coracoid process, coraco-acromial ligament, and acromion) with the subdeltoid fascia. The supraspinous fascia, which covers the supraspinatus muscle, has been removed. The dotted circle represents the outline of the subacromial bursa, established by probing the bursa through the subdeltoid fascia.

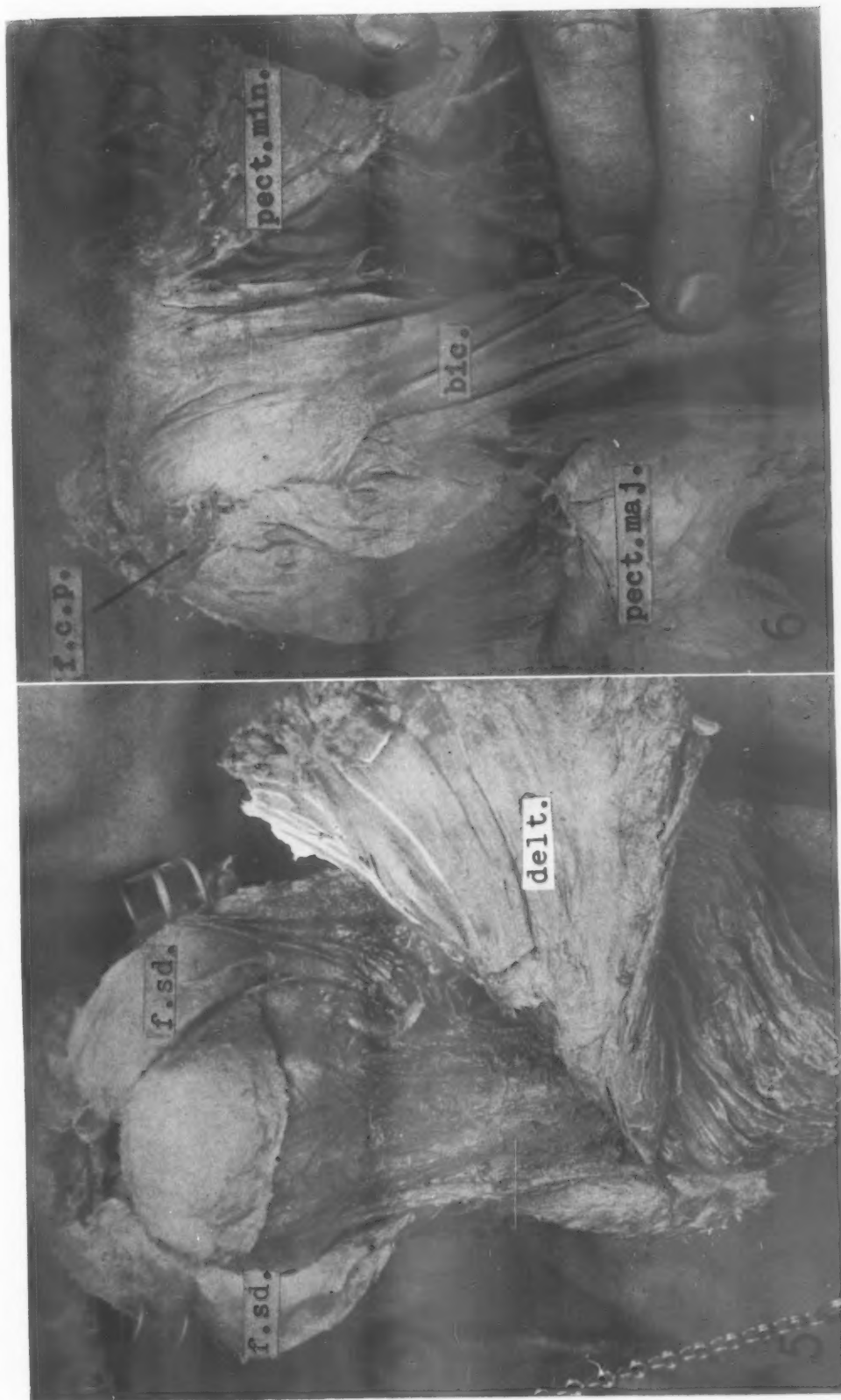


FIG. 6.—Photograph of the ventral aspect of the right shoulder after removal of the deltoid muscle and the clavicle. The subdeltoid fascia has been exposed. Notice its relation to the caput breve of the biceps (*bic.*), and to the costo-coracoid membrane (*f.c.p.*) which has been rolled up onto its junction with the subdeltoid fascia (compare with Fig. 2*b*).

FIG. 5.—Lateral aspect of the subacromial bursa, left shoulder. The deltoid muscle (*delt.*) after being detached from its proximal attachment, has been reflected backwards. The underlying subdeltoid fascia (*f.s.d.*) and coraco-acromial ligament have been cut and the resultant halves have been reflected backwards over the acromion (*trident hook*) and forwards over the coracoid process respectively.

be exposed by removing the subdeltoid fascia, which is rather loosely attached to the outer bursal wall (Fig. 5). In a number of our preparations, however, the subdeltoid fascia consisted of several layers, and in such cases it was difficult to identify the wall of the bursa. Quite a different relation exists between the bursa and the fornix humeri. The coraco-acromial ligament cannot be removed from the subjacent bursa without causing damage to the latter's outer wall. The acromion has a similar relation to the bursa. Like the adjacent part of the coraco-acromial ligament its under-surface is incorporated in the outer wall of the bursa. The remainder of the coraco-acromial ligament (the part connected with the coracoid process) may lie free over the bursa, but it often also forms part of the outer wall of the latter. The relations of the inner wall of the subacromial bursa are as follows. This wall so strongly adheres to the underlying supraspinatus tendon that it is possible to say that the tendon forms part of the inner wall of the bursa. Where the bursa covers the greater tubercle it can easily be lifted from the latter by blunt dissection.

The strong adherence of the bursa to the supraspinatus tendon will cause the inner wall of the former to be displaced with every movement of the latter. During abduction, for instance, the inner wall of the bursa will be drawn medially with the supraspinatus tendon. The position of the outer wall of the bursa is certainly less dependent on the position of the humerus in the shoulder joint, since part of it is formed by the completely fixed fornix humeri, while the remainder of the outer wall is in large part related to the subdeltoid fascia, which during abduction is kept taut by small bundles of the deltoid muscle. The medial displacement of the inner wall of the bursa during abduction will imply a medial shift of its distal line of reflexion, and this shift is presumably facilitated by the loose attachment of the outer wall of the bursa to the subdeltoid fascia.

#### Discussion

It is of great interest to note that Pfuhl (1934) has demonstrated the presence of a layer of cartilaginous tissue covering that part of the undersurface of the acromion which stands in direct relation to the cavity of the subacromial bursa. On the basis of this finding Pfuhl has advocated the conception that the subacromial bursa should be regarded as a true joint between the fornix humeri and the musculo-tendinous cuff. The shoulder joint as a functional entity would thus be composed of a scapulo-humeral "Hauptgelenk" and a subacromial "Nebengelenk". The intervening part of the musculo-tendinous cuff, which is formed by the supraspinatus tendon and the coraco-humeral ligament, is regarded

by Pfuhl as an intra-articular disc. It is a well known fact (see, for instance, McGregor, 1943) that rupture of the supraspinatus tendon may establish a communication of the shoulder joint with the subacromial bursa. It seems that such ruptures usually result from acute overaction of the supraspinatus muscle, but Pfuhl (1934) has observed large perforations of the tendon accompanying severe arthritis deformans of the shoulder joint, so that it would not seem impossible that some cases of rupture of the supraspinatus tendon are caused by repeated trauma of the tendon against the rough articular surface of the humeral head.

There is, indeed, sufficient reason to regard the subacromial bursa as a true joint rather than as an equivalent to the numerous other bursae which assist in the proper functioning of the apparatus of motion. Apart from Pfuhl's argument that a small part of the wall of the bursa is formed by cartilaginous tissue, the following other facts can be advanced in favour of this conception: (1) the subacromial bursa is the only bursa which is known to be able to reduce friction between two skeletal elements (greater tubercle of the humerus versus under surface of the acromion); and (2) the bursa is covered by and attached to a strong aponeurotic fascia, the subdeltoid fascia, which is kept extended during movements by some bundles of the deltoid muscle and by the short head of the biceps. Comparable mechanisms serving to prevent the formation of incarcerated folds in the capsule are formed in many other joints (capsule stretchers).

Although it would thus seem justified to speak of a subacromial joint, it is evident that the joint is an exceptional one functionally and morphologically. With regard to its function, it should be realized that its prime significance lies in the fact that it reduces the conflict which is bound to arise between an exceptionally mobile joint like the shoulder joint and the rigid tissues surrounding this joint. Morphologically it differs from most other joints in that only a very small part of its wall consists of cartilage and that it is largely a synovial sac with, of course, merely a virtual cavity. It follows that a slight proliferation of the wall of the subacromial joint in the course of an inflammatory process may suffice to result in partial or complete obliteration of the joint cavity with consequent anchorage of the musculo-tendinous cuff of the shoulder joint to the completely rigid fornix humeri, a condition which will greatly decrease the range of movements of the upper extremity.

#### Summary

The interest of clinical rheumatology for the periarticular tissues of the shoulder joint, together



with the fact that current textbooks of anatomy fail to give satisfactory descriptions of these tissues, has led the authors to investigate this region anew. The following account is based on dissecting-room material.

A description has been given of the capsule of the shoulder joint and its relation to the fornix humeri (coraco-acromial ligament and acromion). The fornix humeri is part of a much larger fibrous system, the subdeltoid fascia. This fascia anteriorly fuses with the subscapularis fascia, posteriorly with the infraspinous fascia, and laterally to the periosteum of the surgical neck of the humerus. Tendon-fibres of the short head of the biceps fan out into this fascial sheet, whereas muscular fibres of the deltoid muscle insert into it in the disto-proximal direction. Both may serve to stretch this fascial sheet during movements of the shoulder, thus preventing it from becoming enfolded under the fornix humeri. Between the capsule of the shoulder-joint on the one hand, and the fornix humeri and its lateral extension (the subdeltoid fascia) on the other, a bursa has developed—the subacromial bursa. A description has been given of the relation of this bursa to the surrounding tissues. A suggestion is made as to the rôle of the subdeltoid fascia and subacromial bursa in movements of the shoulder.

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#### L'Anatomie Macroscopique des Tissus Périarticulaires de l'Epaule

##### RÉSUMÉ

L'intérêt du problème de la périarthrite huméro-scapulaire, spécialement dans un sens rhumatologique, a conduit les auteurs à une recherche anatomique nouvelle sur la région scapulaire. La capsule de l'articulation huméro-scapulaire et ses relations à l'égard du fornix huméri sont décrites. Le fornix huméri (ligament coraco-acromial et acromion) fait part d'un système aponévrotique plus étendu, c'est à dire, l'aponévrose sous-deltoidienne. Cet aponévrose se confond antérieurement avec l'aponévrose sous-scapulaire, postérieurement avec l'aponévrose du sous-épineux, latéralement avec le périosteum du col chirurgical de l'humérus. Des fibres tendineuses de la courte portion du biceps se diversent dans l'aponévrose sous-deltoidienne, tandis que des faisceaux musculaires s'attachent sur celle-ci dans une direction disto-proximale. Il est bien sûr que les deux radiations font un dispositif d'un appareil de tension pour l'aponévrose pendant les mouvements de l'épaule. Entre la capsule de l'articulation huméroscapulaire et le fornix huméri et son extension latérale se trouve une bourse séreuse, c'est à dire, la bourse sous-acromiale. Les auteurs donnent une description de cette bourse et de ses relations à l'égard du revêtement aponévrotique de l'épaule. L'attention est fixée sur l'intérêt de la fonction de la bourse sous-acromiale et de l'aponévrose sous-deltoidienne pour les mouvements l'épaule.

# A CHECK ON THE ANATOMICAL ACCURACY OF INTRA-ARTICULAR HIP INJECTIONS IN RELATION TO THE THERAPY OF COXARTHROSIS

BY

MARJORIE M. DOBSON

In various countries for many years, orthopaedic surgeons have given intra-articular injections into the hip-joint, for the better study of the anatomy of the joint; especially in relation to congenital dislocations of the hip.

## Review of the Literature

Cornet (1933) insufflated this joint in infants with air and oxygen, and reported on 14 cases of subluxation of the hip-joint in which radiographs taken after the injection showed a very clear definition of the articulation and its capsule.

Various radio-opaque solutions have been used, of which mention may be made of "thorotrast", "abrodyl", "uro-selectan B", "diagnerol", and "tenebryl".

In France, Leveuf and Bertrand (1937) found that most radio-opaque solutions gave satisfactory results in patients chosen from cases of subluxation of the hip-joint. The joint was injected from the lateral aspect, from a point just above the great trochanter of the femur.

Gunnar Wiberg (1939) used a specially prepared solution of perbrodil in making arthrographs from twenty-two normal or nearly normal hip-joints from cases which presented for operation for some other reason. The joint was approached from the anterior, and the needle inserted just below Poupert's ligament, 1 cm. outside the femoral artery. After the head of the femur had been reached by the needle, the point was withdrawn a few mm. before the injection was made.

Thus, most studies in arthrography have been made from the orthopaedic point of view, and preceding operative procedures.

Other investigators have injected the hip-joint for therapeutic reasons. Thus Grant Waugh (1938), having studied the physio-chemical changes occurring in normal synovial fluid after trauma, especially the changes in the hydrogen ion concentration, treated minor joints after injury with intra-articular lactic acid injections. His results were beneficial in a high percentage of cases. Later (1945) Waugh reported on twenty-five cases of coxarthrosis so

treated. Recovery of function and relief of pain occurred in between 50 and 60 per cent. of these.

Warren Crowe (1944) showed the benefit from treatment by intra-articular injections of an acid potassium phosphate solution, in two-thirds of his cases of coxarthrosis. He used the anterior approach in most of his cases.

In France Coste and Morin (1939) had been trying various analgesic solutions intra-articularly for the treatment of coxarthrosis. They came to the conclusion that there was a purely functional relief of the condition.

In America, Tarsy (1938) used 1 per cent. procaine into the hip-joint in the same disease.

It will be noticed from the literature that many observers used combined peri-arthritis and intra-arthritis injections in the treatment of osteoarthritis of the hip-joint. Some used only small amounts of injection fluid, although Grant Waugh and Warren Crowe advise an amount of 20 c.cm. for this joint. Almost all have owned to a few failures in introducing the fluid in its entirety into the synovial cavity. The beneficial effects of these intra-articular injections in the treatment of coxarthrosis have been attributed by these investigators either to the chemical composition, or to the pH of the solution injected, or to the analgesic solution breaking the reflex of painful spasm.

## Discussion

In my opinion the most important part of the injection treatment of coxarthrosis is that the whole capacity of the joint should be taken up by the appropriate solution injected, although this latter must of course have the correct physio-chemical composition and isotonicity. (Analgesic solutions will not be discussed here.)

An amount of fluid equal to the capacity of the joint will exert a centrifugal, equalizing, hydrostatic pressure on the whole synovial membrane and its villi, albeit short-lived owing to absorption.

It is possible that in the earlier stages of osteoarthritis of the hip, and especially in the "rheumatoid" type that also occurs, this sudden equalizing

TABLE 1  
RESULTS OF INJECTING THIRTY-THREE JOINTS WITH CARMINE IN GLYCERINE

Age	Disease	Successful		Unsuccessful		Not seen	Case
		Jelly	Staining	Ilio-femoral ligament	Muscle		
74	Cardiovascular degeneration ..	—	yes	—	—	—	1
74	Cardiovascular degeneration ..	—	—	yes	—	—	2
80	Cerebral thrombosis ..	—	—	yes	—	—	3
80	Cerebral thrombosis ..	—	—	yes	—	—	4
74	Cardiovascular degeneration ..	yes	—	—	—	—	5
73	Cancer of rectum ..	—	—	yes	—	—	6
73	Cystitis ..	—	—	yes	—	—	7
74	Cardiovascular degeneration ..	yes	—	—	—	—	8
73	Cancer of rectum ..	yes	—	—	—	—	9
73	Cancer of rectum ..	yes	—	—	—	—	10
91	Senile ..	—	—	—	yes	—	11
71	Bronchitis and emphysema ..	—	—	—	—	yes	12
84	Senile ..	yes	—	—	—	—	13
84	Senile ..	yes	—	—	—	—	14
73	Myocardial degeneration ..	—	—	yes	—	—	15
73	Myocardial degeneration ..	yes	—	—	—	—	16
76	Cancer of pharynx ..	yes	—	—	—	—	17
76	Cancer of pharynx ..	—	—	—	yes	—	18
85	Bronchial pneumonia ..	yes	—	—	—	—	19
85	Bronchial pneumonia ..	—	yes	—	—	—	20
81	Uraemia ..	—	yes	—	—	—	21
71	Uraemia ..	—	—	—	yes	—	22
64	Bronchial pneumonia ..	—	yes	—	—	—	23
64	Bronchial pneumonia ..	—	yes	—	—	—	24
68	Arterial sclerosis ..	—	yes	—	—	—	25
71	Uraemia ..	yes	—	—	—	—	26
80	Cancer of colon ..	—	yes	—	—	—	27
80	Cancer of colon ..	—	yes	—	—	—	28
64	Cardiovascular degeneration ..	—	—	yes	—	—	29
86	Bronchial pneumonia ..	—	yes	—	—	—	30
69	Advanced paralyses ..	—	—	—	—	yes	31
76	Paget's disease ..	yes	—	—	—	—	32
76	Paget's disease ..	yes	—	—	—	—	33
Totals .. ..		12	9	7	3	2	33
		21		10		2	33

and expanding pressure of isotonic solution will separate congested villi, and in any type of coxarthrosis will facilitate drainage through the villi. In the more chronic cases there may be some stretching of the capsule and temporary separation of eroded cartilages, except in the very advanced cases.

Thus, apart from the physio-chemical action of the fluid introduced, there occurs a threefold effect if sufficient fluid is used. First, there is a gradual replacement of the existing synovial fluid, or a "washing out" through villous absorption; secondly there is an "ironing out" of the synovial membrane; and lastly there may in some cases be a stretching of the capsule.

Over a period of four years, in my own cases of coxarthrosis treated by the acid phosphate solution, I have noticed how often an advanced osteo-

arthrosis, with much contraction of capsule and joint destruction, will "take" only perhaps 10 or 15 c.cm. of solution at the first injections, before back-pressure occurs in the syringe, whereas later the amount retained intra-capsularly may be considerably increased. It is because I feel that the most important factor in treatment of coxarthrosis by intra-articular joint injection is that all the fluid should enter the joint to the full capacity of the joint and that there should be no peri-articular leakage, that I made the following control injections on the cadaver. It may be owned that the results may reflect on the skill of the individual injector of solution; but this will only serve to emphasize the importance of a skilled and experienced technique in this treatment in the living, of coxarthrosis by "acid" therapy.



### Results in the Cadaver

The approach was from the anterior, in these cases, taking a point 1 inch outside the femoral artery, on a line joining the superior border of the trochanter to the pubic ridge.

My first results proved to be of little value, because the contraction of the tissues by the preservative used on the cadaver diminished the size of the joint cavity and made difficult the differentiation of the various layers of muscle, ligament, and capsular structures, by the puncture needle. This was partly overcome by injecting the cadaver within 24 to 48 hours after its arrival from the mortuary.

The question of a suitable dye was the next difficulty, as an aqueous solution was soon absorbed from the joint and dissipated into the surrounding tissues, before the time of dissection of the limb by the students. At length a suitable solution of carmine in glycerine was tried, which, injected hot, was found at the subsequent dissection at the site of injection in the form of a jelly.

Accuracy of the injection was made more difficult in the cadaver by several factors; namely, the additional surface marking necessary for the femoral artery, whose palpation is so useful in the living; and the severe deformities and senility of the greater number of subjects. I also missed the help given by the living patient as to sensitivity of the needle puncture, and changes in sensation during the operation.

TABLE 2  
SUMMARY OF RESULTS

Number of Cases .. .. .	33
Successful .. .. .	21
Unsuccessful .. .. .	10
No result (absorption of dye) .. .. .	2
Percentage of successful results .. .. .	64

### Results

The results are given in the form of Tables. The number of joints injected was thirty-three. Results were considered to be completely successful if the mass of jelly was inside the acetabular cavity of the joint; and moderately successful if there was a red dye staining over the acetabulum cavity, or over the head of the femur. Unsuccessful results were those in which the dye-jelly was in the ilio-femoral ligament, or in the muscles surrounding the capsule (usually the ilio-psoas tendon).

These results may appear to be somewhat disappointing; they show a successful result in 65 per cent. of cases only; but in view of the fact that in the living patient periodic injections are made, of which many at least will be completely intra-capsular, and bearing in mind the above-mentioned difficulties of technique, they are less discouraging than might at first appear. They may possibly explain why, instead of 100 per cent. successful results in intra-articular therapy, there are only perhaps 65 per cent.

### Summary

Results are given of a few consecutive intra-articular hip injections in the cadaver, preceded by a short survey of previous work done in intra-articular injections of the hip-joint.

The method was the anterior approach in these cases; but at present I am making a comparative study of results using the lateral approach.

Thanks are due to Professor Lucas Keene and the Council of the London School of Medicine for permission and facilities to carry out this investigation; also to the laboratory technician and the curator of the Anatomy Department for their assistance in producing suitable material and subjects for injection.

Since writing this article, Bayer and Chayer have reported on 29 cases of hip-injection treatment in osteo-arthritis. The opinion they give as to the benefit of this therapy is partly that discussed above. Messrs. Allen and Hanbury, Ltd., are kindly endeavouring to prepare a more viscous solution of acid phosphate, and, since December, 1947, have been undertaking research on these lines for me.

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### Vérification de la Précision Anatomique des Injections Intra-articulaires de la Hanche en Relation avec le Traitement de l'Arthrite de la Hanche

#### RÉSUMÉ

Cet article donne les résultats de trente-trois injections consécutives dans l'articulation de la hanche sur le cadavre, ainsi qu'une brève revue des travaux antérieurs portant sur les injections dans l'articulation de la hanche. Les résultats ont été considérés comme excellents lorsque la masse de gelée se trouvait dans la cavité acétabulaire de l'articulation; et comme assez bons lorsque l'on constatait une coloration rouge au-dessus de la cavité acétabulaire ou au-dessus de la tête du fémur. Les mauvais résultats étaient ceux dans lesquels la gelée colorée se trouvait dans le ligament ilio-fémoral, ou dans les muscles entourant la capsule (généralement le tendon du psoas). La voie d'accès choisie était la voie antérieure, mais l'auteur procède actuellement à une étude comparative des résultats obtenus par la voie d'accès latérale.

Les résultats n'ont été excellents que dans 65 pour cent des cas; mais si l'on considère le fait que sur le malade vivant on procède à des injections périodiques, et si l'on tient compte de la difficulté de la technique, cette proportion est moins décourageante qu'elle ne semble *a priori*.

# THE PROBLEM OF ARTHRITIS IN SWITZERLAND\*

BY

A. BÖNI

*Section on Physical Medicine University Hospital, Zürich*

The establishment of general measures of prophylaxis and therapy for arthritis has become in the last few years one of the serious concerns of the public and the authorities in Switzerland. Up to the present time, due to the relatively high standard of living of the Swiss working class, the labourers had been in a position to finance their treatment in most instances by their own means and with the help of their health insurance policies. As for the disabled and handicapped, the natural solution for them, in a predominantly agricultural population, was to be taken care of by their own families. The authorities, therefore, as represented by the Federal Health Department, have hitherto been given but small incentive to approach the problems of non-epidemic diseases.

Since the two world wars, however, with their sequels of high cost of living, of industrialization, and of rapid increase in the urban population, there has been a growing awareness of the problems with which the whole community is confronted due to the extent of chronic disabling diseases of the arthritic type.

Bruck (1939), former resident physician at the University Clinic for Physical Therapy in Zürich, produced interesting statistics about incidence and social effects of arthritis in Switzerland. The figures mentioned subsequently are taken from his publication. They are based mainly on a study of 93,750 reports of sickness among members of three organizations of national importance. These organizations, which include a typical portion of the average Swiss population, are: (a) the Zürich Trade Health Insurance Co. † (reports of illness of 11,300 men and 8,100 women from 1929 to 1931) (see Table); (b) the St. Gall Christian Social Health Insurance Co. ‡ (reports of illness of 21,950 men and 29,400 women from 1929 to 1931); (c) the health service of the Swiss Federal Railways § (reports of

33,000 employees from 1925 to 1935). Cases of rheumatoid arthritis, osteo-arthritis, and fibrositis were included in this study under the name of arthritis or chronic rheumatic diseases, without further specification of diagnosis.\* The statistical material thus collected particularly showed the influence of the three factors of occupation, age, and season on the incidence of the diseases of the arthritic group.

## **Influence of Occupation, Age, and Season on Arthritis**

### **Occupation**

*Women.*—The incidence of arthritis among the females of various occupations who reported sickness to the Zürich Trade Health Insurance Co. was as follows: 14.29 per cent. of the laundresses showed arthritic affections; 8.00 per cent. of the ironers; 7.43 per cent. of the housewives (this does not include maids); 3.57 per cent. of the typists; 2.33 per cent. of the seamstresses. Diseases and accidents connected with pregnancy and childbirth were not included in this calculation.

The female cases of the St. Gall Christian Social Health Insurance Co. presented a similar picture, with the highest incidence of arthritis appearing among the laundry workers (8.01 per cent.). The women working in agriculture ranked second in this series with an incidence of 5.39 per cent.

*Men.*—A study of the male cases of these two health insurance companies showed the following facts: (a) dyers and finishers had the highest incidence of arthritic conditions (8.08 per cent.); (b) porters ranked second with 7.89 per cent. incidence; (c) office clerks and weavers had an incidence of only 2.78 per cent. and 1.71 per cent. respectively.

Among the personnel of the Swiss Federal Railways, 15.41 per cent. of the outdoor workers, 8.5

\* Read at the First European Congress of Rheumatism at Copenhagen, Denmark, September 4 to 8, 1947.

† Gewerbe Krankenkasse der Stadt Zürich.

‡ St. Galler und Christlich-soziale Krankenkasse.

§ Schweizerische Bundesbahnen.

\* It would add materially to the value of such observations as are contained in this article if the three main types of chronic rheumatism were separated into rheumatoid arthritis, osteo-arthritis, and fibrositis, since they differ in aetiology and pathology and to some extent in treatment. Conclusions obtained from a combined grouping are apt to be misleading.—Editor.

per cent. of those who worked part of the time indoors and part of the time outdoors, and 3.01 per cent. only of those who worked in offices were reported to be afflicted with some arthritic condition.

These figures stress the importance of environmental factors in the aetiology of arthritis. It seems evident, for instance, that the great dampness in the working rooms of laundresses, ironers, dyers, and finishers accounts for the high incidence of arthritis in these vocations. Porters, farmers, and other outdoor workers, who are exposed both to trauma and inclement weather, are in a particularly unfavourable situation also.

On the other hand, low incidences are found among the typists, seamstresses, and office clerks who work in regulated atmospheric conditions with a minimum of mechanical strain. The low percentage incidence among weavers acquires full significance when it is recalled that most weaving mills are carefully air-conditioned, the air being maintained relatively dry and at a temperature of 22° to 24° C. (71.6° to 75.2° F.).

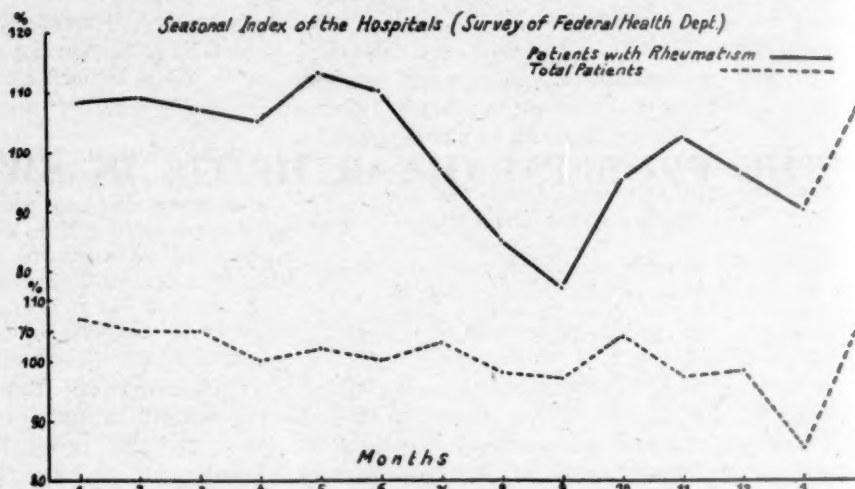
TABLE  
INCIDENCE AMONG MEMBERS OF ZÜRICH TRADE  
HEALTH INSURANCE CO., PERCENTAGE OF ALL SICKNESS

* Men					† Women				
Age, yr.	Arthritis	Tuberculosis	Others	Total	Arthritis	Tuberculosis	Others	Total	
0-14	0.17	1.41	98.42	100	0.51	1.52	97.97	100	
15-29	9.10	0.91	89.99	100	6.27	1.22	92.51	100	
30-39	15.95	1.02	83.03	100	8.72	0.93	90.35	100	
40-49	18.79	0.42	80.74	100	8.88	0.95	90.17	100	
50-64	18.59	1.23	80.18	100	6.37	1.29	92.34	100	
15-64	14.18	0.92	84.26	100	4.41	1.04	93.95	100	

\* Bruck, Index No. 63

† Bruck, Index No. 64

The Table shows a comparison between the incidence of arthritis, of tuberculosis, and of the other diseases with respect to the age of the patients. In contrast to tuberculosis, which appears much earlier, arthritis reaches its maximum of incidence in men and women of 50 to 60 years of age. This is the age at which, in addition to hormonal and metabolic disturbances, the external noxious agents have had time to develop their cumulative effects in the organism.



**Seasonal Incidence.**—There are two peaks of incidence, one in the spring and one in the autumn (see Figure). These peaks coincide with the periods of maximal occurrence of "colds", upper respiratory infections, tonsillitis, and streptococcal pharyngitis. This observation agrees with both the theory of streptococcal aetiology of arthritis and the theory of virus infection proposed by von Neergaard ("catarrhal rheumatism").

The results of the statistical studies on arthritis that were made in Switzerland concur with the opinion that infectious factors (seasonal incidence) and constitutional factors (age incidence), as well as environmental factors (vocational incidence), are of primary importance in the production of this condition.

#### Socio-economic Effects of Arthritis in Switzerland

Much more emphasis has been placed so far on the protection of the community against the effects of tuberculosis than against the effects of arthritis. It is interesting, therefore, to compare the damages of social significance brought about by each of the two diseases.\*

**General Incidence in Switzerland.**—Expressed in percentages of the incidence of all diseases, the cases of arthritis represent 16.2 per cent., and the cases of tuberculosis only 0.45 per cent. The ratio of tuberculosis to arthritis is 1 : 36.

**Unemployment due to Illness.**—In the personnel of the Swiss Federal Railways, arthritis accounts for 16.4 per cent. of the total hours of absence due to illness, whereas tuberculosis accounts for only 3.7 per cent. of this time. In other words, 4.4 times more working hours are lost as a result of arthritis than as a result of tuberculosis.

\* See also the June issue of the *Annals*, in which Dr. O. Savage discusses Dr. P. S. Hench's observations on this subject.—Editor.



**Financial Losses.**—Every year the Swiss national economy loses important sums of money because of tuberculosis but significantly more because of arthritis.

*Financial Losses due to Tuberculosis.*—Loss of work because of death due to tuberculosis amounts to 5,000,000 to 7,000,000 Swiss francs yearly. Loss of work because of disability due to tuberculosis has amounted to 35,000,000 to 40,000,000 Swiss francs yearly. The federal government, the cantons, the communes, and the individuals have spent 18,000,000 to 19,000,000 Swiss francs yearly for treatment, hospitalization, caretaking, and tuberculosis organizations.

*Financial Losses due to Arthritis.*—Loss of work through sickness of short duration has cost 40,000,000 to 45,000,000 Swiss francs yearly; loss of work through premature retirement, 200,000,000 to 220,000,000 Swiss francs yearly; expenditures for treatment, 15,000,000 to 20,000,000 Swiss francs yearly.

It might be of interest also to compare the total financial losses imposed on the Swiss population by the two chronic diseases, arthritis and tuberculosis, with the relatively large sum of money expended by the country for purposes of military preparedness. The total loss due to tuberculosis is 58,000,000 to 66,000,000 Swiss francs yearly, which averages 15 Swiss francs per head above the age of 15. The total loss due to arthritis is 225,000,000 to 280,000,000 Swiss francs yearly, which averages 85 Swiss francs per head above the age of 15. The current expenditures for army purposes are 300,000,000 to 400,000,000 Swiss francs yearly. These facts compel us to conclude that arthritis, which provokes economic losses of a magnitude approaching that of the price paid for national security, must be a matter of national concern, and that this ailment deserves indeed to become the objective of a thorough and comprehensive programme of action.

#### Outline of a Health Service for Arthritis

The possibilities of influencing arthritic conditions are more numerous than generally is admitted, but a specific therapy is, of course, out of the question for the time being.

In the few cases where focal infection is obvious, focal sanitation and the use of the modern antibiotics are the natural measures of treatment. But in most other forms the basic infection (due to cocci or viruses) remains occult. The infectious agents in these cases seem very often to be ubiquitous and to become pathogenic under the influence of external insults, of general endocrine and metabolic changes, or of local disturbances in the organism. The first problem in dealing with these conditions is that of keeping under control the reactions of the organism

to banal factors, such as cold, humidity, micro-traumatism, and ubiquitous micro-organisms. The goal of the treatment is to raise the non-specific resistance of the body, and the most efficient means for this purpose are, in our opinion, the general procedures of physical therapy: baths, fever therapy, light therapy, exercise, massage, and so forth. These are the weapons of what we term reaction therapy and reaction prophylaxis. We consider them of paramount general (and not only symptomatic) value in the approach to arthritic conditions, provided that they are applied by medical men of unquestionable experience in the field and by thoroughly trained therapists. The same physical agents, to which we must not forget to add the climatic and spa therapy, have also a beneficial regulating action on the hormonal and metabolic disturbances often observed in connexion with arthritis.

There is good reason to believe, therefore, that physical therapy, including also spa and climate therapy, which already plays the central part in the fight against arthritis in Switzerland, will continue to do so in the extensive programme of action that is being developed. Drug therapy, of course will not be neglected, but since it raises no special problem of organization, it will not be discussed further in this paper.

Any health service organization aiming at a comprehensive approach to the problem of arthritis, must have a division of preventive medicine and a clinical division working in close association with a specialized social service for arthritis.

**Division of Preventive Medicine.**—In the division of preventive medicine, both medical and social workers have to co-operate with the authorities in the establishment of: (1) more and better ways of eliminating the environmental factors which play a role in the development of arthritis (passive, or exposure prophylaxis); (2) more and better means of raising the power of resistance of the population against those same factors and the agents of banal infections (active, or reaction prophylaxis).

**PASSIVE PROPHYLAXIS.**—The following activities of the division are connected with the first purpose (passive prophylaxis).

*Surveys of Housing and Working Conditions.*—The elimination of dampness, the protection against draughts and sudden changes in temperature, are of over-riding necessity both in homes and in plants (modern concrete tenements are particularly objectionable in this respect). The workers, furthermore, must be protected against trauma, and particularly repeated microtrauma. This implies working under favourable postural conditions and with improved mechanical equipment.

*Vocational and Pre-vocational Series Examinations by Specialists in Arthritis.*—The detection of the subclinical and threshold cases is here of paramount importance. It is senseless, for instance, to allow an asthenic youth or a boy with a spinal insufficiency to choose an occupation requiring heavy bodily work. It is equal nonsense to let girls with a history of an early attack of rheumatism earn their living as laundresses or kitchen-maids.

**ACTIVE PROPHYLAXIS.** As regards the second purpose of the division (active prophylaxis) various measures, as previously mentioned, have been recognized to be of value in increasing the power of non-specific resistance of the organism. Such measures are, for instance, the practice of cold hydrotherapy and of heliotherapy, the use of the Finnish bath ("Sauna"), the practice of sport and gymnastics under medical control, and preventive annual visits in a spa or in a mountain resort.

It is the duty of officials and of private organizations, to see, with the help of the arthritis service, that the necessary facilities are provided and are used in accordance with sane medical concepts.

**Clinical Division.**—As soon as the arthritic condition becomes evident, treatment must be inaugurated with the utmost diligence. The general practitioner comes into action first, and he carries the widest responsibility for the patient's future. If he has any doubts concerning the diagnosis, or if he needs therapeutic advice, or if he fails to have the necessary therapeutic facilities, he must have every opportunity to refer his patient to a specialist or to an approved arthritis clinic.

The functions of the arthritis clinic will now be examined in some detail. They are those of diagnosis, treatment, and evaluation of vocational ability or of need for further care.

**Diagnosis.**—Anybody dealing with arthritic conditions knows how difficult it often is to establish an accurate differential diagnosis in this particular group. Off-hand diagnoses are always dangerous in the arthritic section. All modern facilities must be at hand if reliable examinations are to be made. The "mobile equipment" which proved to be useful for tuberculosis cannot be thought of for arthritis.

**Treatment.**—The direction of the treatment is assumed by the clinic only on the wish of the general practitioner, and to secure for the patient the benefits of more elaborate equipment. The physicians of the clinic have to administer the medical treatment, to prescribe the instructions for physical and occupational therapy, and occasionally to refer the patient to another department for, say, orthopaedics or x-ray therapy. The backbone of the therapeutic programme, indeed, is in most instances the application of physical therapy.

As regards the high costs of this form of treatment, it should be remembered that the best available therapy is in final analysis always less expensive than an incomplete or imperfect treatment.

**Evaluation of Vocational Ability and of the Need of Further Care.**—As an impartial party, disposing of an up-to-date diagnostic equipment, the arthritis clinic is in the best position to decide whether, when, and to what extent a patient can resume his former occupation. In several instances, furthermore, the question arises of a continuation of treatment or of a convalescent stay, in a sanatorium for arthritics, in a spa, or in a climatic resort. The answer to this can only be the result of careful medical assessment. This is a work of selection, in which the physician must keep in mind that the interest of the community as well as of the patient himself requires that those who do not need it, or for whom it may even be harmful, be restrained by persuasion from such therapy.

**Social Service.**—Social workers in this field must have a specialized training to be able to understand and to solve the very particular problems facing the arthritic.

A qualified report about the detrimental factors among a patient's housing and working conditions is of invaluable help to the physician in his dealing with many a case of arthritis. The social worker must be prepared to do this kind of investigation and to suggest the necessary measures of hygiene.

If the patient is unable to resume his former occupation on account of unavoidable detrimental conditions in his work or on account of permanent disabilities of his own, the social service has to help him find adequate new working opportunities and achieve his vocational rehabilitation.

In the cases where one of the following forms of therapy has been specifically indicated by the physician, the social service must be in a situation to provide the patient with all information concerning sanatoriums, spas, or climatic resorts, and to secure his admission in an ethical institution.

In keeping contact with present and past patients the social service has the best opportunity of collecting data and establishing statistics on the effects of the measures taken with its help or under its supervision. These findings, in turn, will be the rational basis for the subsequent activity of the entire arthritis organization.

#### Concluding Remarks

This is a far-reaching programme, the foundations of which are being built in Switzerland. Yet, it must be emphasized, in conclusion, that the whole plan is to be carried out on a voluntary basis. The liberty of the patient and the privileges of the

general practitioner are to be respected in all circumstances. The arthritis service will place its resources and its qualified personnel at the disposal of those only—physicians, patients, communities—who apply for its help.

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## Le Problème de L'Arthrite en Suisse

## CONCLUSIONS

Pendant les dernières années la Suisse s'est occupée sérieusement à établir des mesures prophylactiques et thérapeutiques contre l'arthrite.

Les statistiques de deux compagnies d'assurance sur la santé dans le commerce à Zurich montrent, chez les femmes, une haute incidence d'arthrite chez les blanchisseuses, et une incidence peu considérable chez les couturières. Chez les hommes on trouve la plus grande incidence d'arthrite chez les teinturiers et les finisseurs, et la moindre incidence chez les employés de bureau et chez les tisserands. Parmi les employés des chemins de fer fédéraux suisses les employés de bureau sont plus rarement frappés d'arthrite que ceux qui travaillent au dehors.

Les statistiques montrent l'importance dans l'étiologie de l'arthrite d'étudier les influences externes: par exemple, les blanchisseuses et ceux qui travaillent dans des conditions d'humidité, et les facteurs, les fermiers et ceux qui travaillent au dehors, tous ceux travaillent dans des conditions peu favorables; de l'autre côté il y a les dactylographes, les couturières, les employés de bureau et d'autres chez qui l'incidence d'arthrite est assez basse.

Deux fois par an, en printemps et en été, on rencontre la majorité de cas d'arthrite. C'est en printemps et en été qu'on rencontre aussi la majorité de cas de "rhume", des infections des voies respiratoires hautes, les angines, et les pharyngites streptococcales.

La proportion de la tuberculose à l'arthrite en Suisse est dans le rapport de 1 à 36. On donne aussi les chiffres pour les pertes financières dues à ces maladies. On décrit un projet pour une organisation médicale contre l'arthrite, qui est divisée en deux parties: (1) la division de la médecine préventive, qui cherche à enlever les conditions externes qui contribuent à la haute incidence de l'arthrite, et à renforcer la résistance de la population aux maladies; (2) la plus grande responsabilité dans la division clinique reste sur le médecin praticien. On n'entreprend de traitement dans la clinique que sur son désir, et pour assurer pour le malade les avantages d'un équipement plus complet. On appuie sur l'importance des "social workers" pour garder le contact avec les malades.

Ce projet doit être accompli à choix libre. Les ressources et le personnel du service de l'arthrite seront mis à la disposition de ceux—médecins, malades, communautés—qui solliciteront de l'aide.



## THE HEBERDEN SOCIETY

In a short communication read before the Heberden Society recently, Mr. W. D. Coltart described the condition of degenerative patello-femoral arthritis. Degenerative changes in the patellar articular cartilage are common post-mortem and operative findings, and well marked patello-femoral crepitus is often observed in symptomless knees. Occasionally the condition becomes painful and disabling and cases can be divided into three clinical groups: (1) arthritis of the patello-femoral articulation occurring after a fracture of the patella; (2) a post-traumatic condition without definite fracture; (3) cases of apparently spontaneous origin.

The affection can be recognized by a definite syndrome of: (a) characteristic pain in the patellar area, (b) patellar tenderness, (c) pain referred to the patello-femoral region on active extension of the knee against resistance, (d) complete relief of painful symptoms when the knee is immobilized in plaster and the immediate recurrence of these symptoms when the plaster is removed, (e) a rather remarkable absence of sign of generalized arthritis of the knee, and no radiographic changes.

Conservative treatment is unsuccessful in the majority of cases, and patellectomy is often indicated. At operation the articular cartilage of the patellar is seen to be fibrillated, tufted, and discoloured. Later there is erosion of the cartilage and eburnation of the underlying bone.

Although degenerative patello-femoral arthritis in its turn may give rise to a true osteo-arthritis of the knee, it should at first be regarded as a clinical entity and not simply as part of a generalized affection of the whole joint.

Professor Östen Holsti, University of Helsinki, read a paper on an epidemic of Reiter's disease. The data for it had been collected by his former Registrar, Dr. I. Paronen, and will be published by him as an academic thesis in a supplement to the *Acta Medica Scandinavica*. The following is a summary of Professor Holsti's paper.

### An Epidemic of Reiter's Disease

In the summer of 1944 an epidemic of Flexner dysentery raged in Finland and affected about 150,000 persons, mostly soldiers on the eastern front. An outbreak of Reiter's disease followed

in 0.20 per cent. of the dysentery patients. Within a few months more than 300 cases of Reiter's disease were seen, the great majority in soldiers who as a rule were young. A few women attending hospital or other military departments were, however, also affected. About two-thirds of the cases developed within three weeks, and four-fifths within one month of the onset of dysentery, some even before the latter had cleared up. In the remaining cases the interval was longer, even up to three months.

Most cases were accompanied by fever. This was at times of a septic, at times of a continual chronic type. In some cases the fever disappeared after a few days, only to return later. In two-thirds of the cases the fever disappeared definitively within two, and in four-fifths of the cases within three, weeks. Occasionally we had cases that presented fever for several months.

The erythrocyte sedimentation rate was normal in a few cases. In most cases it was raised to a variable extent, even up to 140 mm. per hour.

Various degrees of leucocyte response were also evenly distributed in our material. In the septic cases values up to 18,000 were seen. In others there was no rise in the granulocytes, the differential blood picture showing increased values only of the lympho- and monocytes. In about a third of the cases there was a marked increase—up to 30 per cent. of the eosinophilic cells, a higher figure than in any other form of arthritis I know of. A slight degree of anaemia was present in some cases.

In the beginning the disease was mostly monosymptomatic. Evenly distributed monosymptomatic forms occurred as eye, joint, and genito-urinary syndromes. Bisymptomatic syndromes appeared in a quarter of the cases. Rarely the disease was trisymptomatic from the beginning. Within three weeks the clinical picture changed completely so that about 70 per cent. were trisymptomatic and about 90 per cent. at least bisymptomatic. Still later, within a period of two or three months, all remaining cases were again of the monosymptomatic type, but now they all presented the picture of a joint disease (Fig. 1).

Fig. 2 shows that the knees and ankles were most frequently affected, but any joint might be the seat of a lesion. A combination of pains and swelling

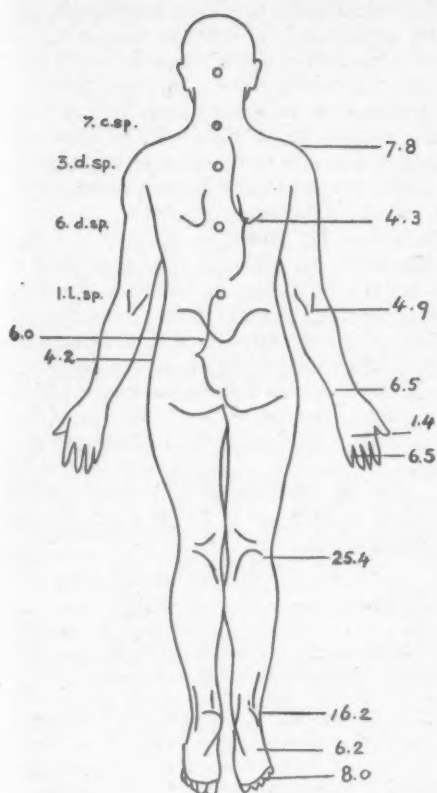


FIG. 1.—The clinical syndromes: U = genito-urinary; E = eye; J = joint.

were the commonest syndrome. Large hydrops without pains occurred, however, not infrequently in the knee-joints. Tendo-vaginitis occurred in some cases with or without simultaneous joint lesions. The skin over the affected joints had often a dirty greyish colour. The clinical course of the arthritis was somewhat like that seen in rheumatic fever, as one joint after the other became rapidly affected. It differed, however, in this respect, that at the time when new joints became affected the older lesions had not yet healed. In this respect the arthritis in Reiter's disease was more like that seen in rheumatoid arthritis, especially as there was a tendency to fibrous ankylosis, most marked in the finger joints.

A simple acute conjunctivitis was the most common eye lesion. Kerato-conjunctivitis, iritis, kerato-iritis, and ulcer simplex corneae were also seen, although infrequently. In a few cases a sensation of grit in, and water of the eye were the only eye symptoms complained of.

The most frequent genito-urinary lesion was urethritis simplex. Erythema penis was the next most frequent. Bladder and kidney lesions, pro-



FIG. 2.—Distribution of joint lesions (± tendo-vaginitis).

statitis, orchitis, and epididymitis occurred also, but infrequently. In a few cases there was no urethritis.

Smears from the various secretions never showed any pathogenic bacteria. The serological reactions for known infections were all negative, with the exception of agglutination to Flexner dysentery, which was positive in a variable degree.

In the great majority of cases there was an apparent tendency to spontaneous recovery from all symptoms, although relapses were frequently noted before the final recovery set in. Relapses have been seen to take place even after intervals of a few years. When the patients have become familiar with the significance of their symptoms they began in many cases to realize that they probably had had the disease before, even as long as ten or fifteen years earlier, although it had been unrecognized.

Although our cases occurred in connexion with Flexner dysentery it cannot be excluded that other intestinal infections might be able to cause Reiter's disease. Manson-Bahr seems to believe that Reiter's disease is not new, but another name for polyarthritis enterica. My mind is still quite open in regard to the pathogenesis. I do not know, in spite of our large epidemic, whether Reiter's disease is a disease *sui generis* or a syndrome developing in certain susceptible persons in association with various infections, perhaps even extra-intestinal ones. That a certain susceptibility or state of allergy is present is seen from the frequent occurrence of eosinophils in the blood as well as in the eye- and genito-urinary secretions in these patients.

The usual symptomatic therapeutic measures used in acute arthritis were given to all patients. Sulphonamides and penicillin were tried in the more difficult cases. The tendency towards spontaneous recovery, however, made any interpretation very

difficult. We felt that none of these measures had any specific value in treatment. Fever treatment was tried in the later state of the epidemic and it seemed to have a value greater than the above-mentioned drugs. During my stay in London I have become acquainted with the effect of Kettering hypertherm in a case of Reiter's disease, and the effect seemed to be still better and more dramatic than what was seen in our cases when the fever was produced with typhoid vaccine given intravenously.

#### Compte-rendu d'une Réunion de la "Heberden Society"

##### RÉSUMÉ

W. D. Coltart a divisé les cas d'arthrite dégénérative fémoro-rotulienne en trois groupes: arthrites de l'articulation fémoro-rotulienne (1) après fracture de la rotule; (2) post-traumatiques sans fracture; (3) apparemment spontanées. La maladie pouvant être identifiée

par: (a) douleur dans la région rotulienne; (b) hypersensibilité rotulienne; (c) douleur rapportée à la région fémoro-rotulienne lorsque le genou est porté en extrême contre une résistance; (d) soulagement des symptômes par immobilisation et réapparition de ces symptômes lorsqu'on enlève le plâtre; (e) absence d'arthrite généralisée du genou et de modifications radiographiques. Le traitement conservateur échoue généralement et il est souvent nécessaire d'enlever la rotule.

Le Professeur O. Holsti a décrit une épidémie de maladie de Reiter en Finlande chez 0.20 pour cent des malades atteints de dysenterie bacillaire au cours d'une épidémie antérieure. La Fig. 1 montre la répartition des symptômes génito-urinaires, oculaires, et articulaires, et la Fig. 2 la répartition en pourcentages des articulations atteintes. On a appliqué le traitement symptomatique habituel, avec sulfamides et pénicilline pour les cas les plus graves; mais on n'a pas eu l'impression qu'aucune de ces mesures ait une valeur spécifique. La pyrétothérapie semblait plus efficace. L'épidémie sera plus complètement décrite par le Dr. I. Paronen dans *Acta Medica Scandinavica*.



## ABSTRACTS

[This section of the ANNALS is published in collaboration with the two abstracting Journals, Abstracts of World Medicine, and Abstracts of World Surgery, Obstetrics and Gynaecology, published by the British Medical Association. The abstracts are divided into the following sections: acute rheumatism; chronic articular rheumatism (rheumatoid arthritis, osteo-arthritis, spondylitis, miscellaneous); sciatica; gout; non-articular rheumatism; general articles. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. Not all sections may be represented in any one issue.]

### Acute Rheumatism

**Experimental Anaphylactic Lesions of the Coronary Arteries of the "Sclerotic" Type, Commonly Associated with Rheumatic Fever and Disseminated Lupus Erythematosus.** RICH, A. R., and GREGORY, J. E. (1947). *Bull. Johns Hopk. Hosp.*, 81, 312.

Intimal and medial lesions of the coronary arteries commonly result from rheumatic fever. Similar lesions are seen in periarteritis nodosa. The authors and other workers have shown that lesions of various organs in man and animals, closely resembling lesions of rheumatic fever and periarteritis nodosa, may be, and sometimes are, caused by antigen-antibody reactions occurring in protracted anaphylactic states. The following observations are taken to support the views already given. Forty-five male albino rabbits (average weight 2 kg.) were sensitized by large intravenous injections of horse serum. They all became skin-sensitive in varying degrees. They were killed 17 to 364 days after the first injection. The coronary arteries and arteries of other viscera were studied microscopically. Eighteen rabbits had lesions of the coronary arteries showing all stages and degrees as in rheumatic fever, and "serum sickness"; others had "serum sickness" without coronary lesions. The rabbits had received varying doses of antigen; 16 of them were killed 19 to 46 days after the first injection. Similar lesions were found in arteries other than the coronaries in some of the sensitized animals. Eighteen control rabbits were free from coronary lesions after 86 to 134 days. Various phenomena seen in disseminated lupus erythematosus occur in protracted anaphylactic reactions. In disseminated lupus erythematosus even in children, lesions of the coronary arteries occur which are similar to those seen in rheumatic fever and periarteritis nodosa, and in animals with experimental "serum sickness".

[The photographs accompanying this paper are good.]  
D. M. Pryce.

**Liver Changes in Rheumatic Fever.** (Изменение печени при ревматизме.) TOLGSKAIA, M. S. (1947). *Ark. Patol.*, 9, 29.

Although many clinical observations deal with the influence of rheumatic fever on liver function, there are no satisfactory descriptions of corresponding anatomical changes in that organ. The present investigation is based on post-mortem material of patients who died at ages of 3 to 69 years. Almost all the deaths were caused by recurrent heart disease; in only 2 cases did death occur

after the first rheumatic attack. [The number of cases examined is not stated.]

The macroscopic changes in the liver were uniform: chronic venous congestion with "nutmeg" appearance, fatty infiltration, and cloudy swelling. Histologically, venous congestion with a diffuse or focal infiltration of fibroblasts around the central veins and interlobular vessels and in the connective tissue was seen. Perivascular histiocytic infiltration was more pronounced in acute cases. In chronic cases sclerotic changes dominated. The endothelium showed oedematous changes, the walls of the vessels a partial or complete necrosis and a perivascular round-cell infiltration. The changes in the liver were parallel with those in the heart muscle. The author considers the histiocytic infiltration and necrosis of the walls of the vessels to be caused by the rheumatic infection itself, whereas the oedema, the sclerotic changes in the vessels and in the interlobular tissue, the atrophy of liver lobules, the fatty infiltration, and pigimentary changes were the result of the heart failure. No changes corresponding to "Aschoff bodies" in the heart were found. Oedema of the interlobular tissue and the overfilling of the lymphatic vessels are attributed to the venous congestion. The author, however, believes that there is also an active secretion by the lymphatic endothelium as a reaction to the damaging influence of a virus.  
J. Flaks.

**Vascular Lesions in Rheumatic Fever.** LAIPPLY, T. C., and O'NEILL, J. B. (1947). *Quart. Bull. Nihwest. Univ. med. Sch.*, 21, 211.

Lesions considered to be characteristic of acute rheumatic fever have been described in the heart, aorta and other blood vessels, subcutaneous tissue, joints, lungs, and pleura. Changes in organs other than the heart are thought to be primarily vascular in origin, and thus rheumatic fever is considered to be a disease of the cardiovascular system. The specific lesion is the Aschoff nodule.

Experimentally the lesions of acute rheumatic fever have been reproduced in rabbits by various techniques. In the development of hypersensitivity to horse serum, it has been noted that the nuclei of vessel muscle-cells may alter and be indistinguishable from the nuclei of Aschoff cells. Similar vascular muscle-cell changes were seen microscopically in sections from the heart taken from 22 patients dying of acute rheumatic heart disease. In all, 56 cases were examined, 34 being controls. Sections of the heart and other organs were examined microscopically after fixation in 4% formaldehyde and staining

with haematoxylin and eosin. All the cases of acute rheumatic fever showed alterations of the muscle-cell nuclei of the small cardiac arteries and veins, with a striking resemblance to Aschoff cells. Such changes have not been reported before, and were not seen to a comparable degree in the controls. The changes were not observed in organs other than the heart.

The fact that similar changes occur in the nuclei of cardiac blood vessels as part of a hypersensitivity reaction in rabbits and as a part of human rheumatic fever lends support to the view that allergy is an aetiological factor in rheumatic fever. [The conclusion drawn is only speculative, though the findings are suggestive. Vessel changes of a local nature may have a local cause of origin, though they may be part of a general sensitivity reaction.]

D. P. Nicholson.

**Plasma-volume Determinations in Rheumatic Subjects during Oral Salicylate Therapy. Report of a Case with Severe Hemorrhage.** YORK, C. L., and FISCHER, W. J. H. (1947). *New Engl. J. Med.*, 237, 477.

The plasma volume in 6 patients with rheumatic fever and 1 with rheumatoid arthritis was studied to check a suggestion by Jager and Alway that the plasma volume was increased during intensive salicylate therapy. In 6 cases prolonged salicylate therapy produced an average rise of 9% in plasma volume. In 1 case a big rise was associated with clinical evidence of increasing heart failure. The authors suggest that this rise is due to excessive sodium intake. It was also found that a plasma salicylate concentration of about 35 mg. per 100 ml. was associated with a reduction in prothrombin activity. In 1 case, described in detail, marked hypoprothrombin-aemia was the cause of severe haemorrhage and a corresponding reduction in plasma volume.

H. F. Turney.

**Use of Penicillin in the Treatment of Carriers of beta-Hemolytic Streptococci Among Patients with Rheumatic Fever.** GOERNER, J. R., MASSELL, B. F., and JONES, T. D. (1947). *New Engl. J. Med.*, 237, 576.

Since November, 1945, intramuscular penicillin (10,000 units two-hourly day and night for 10 days to a total of 1.2 mega units) has been given to all patients admitted to the House of the Good Samaritan, Boston, with acute streptococcal infections and to all carriers of haemolytic streptococci. All streptococci isolated have been grouped and typed [*sic*] by the Lancefield capillary precipitin technique, and assayed for penicillin sensitivity. During the treatment with penicillin, throat cultures were prepared thrice weekly, then "daily from 1 to 2 weeks after treatment, and then with gradually decreasing frequency to a routine weekly schedule". Antistreptolysin O titres and erythrocyte sedimentation rates were determined at two-monthly intervals.

Results of penicillin treatment are described in a series of 20 patients [apparently rheumatic children] from whose throats *Streptococcus haemolyticus* was isolated. Strains from 16 patients were of Group A and comprised 7 different types, the remaining 4 not being A, C, or H [it is not clear why H and not G typing serum was used; see Mackie and McCartney, *Handbook of Practical Bacteriology*, Edinburgh, 1945, p. 339]; penicillin sensitivity varied from 0.06 to 0.006 units per ml. (minimal inhibitory concentration, M.I.C.). Before penicillin treatment, 2 to 53 cultures per patient were taken over periods varying from 4 to 190 days; in 13 patients the proportions of positive cultures varied from

60 to 100%, with one exception (53 cultures: 17 positive, 30%). After treatment with penicillin alone (15 patients) 7 to 40 cultures per patient were taken over periods varying from 20 to 190 days. From 3 cases only were positive cultures obtained: (1) 2 out of 15 cultures over 77 days; group A, type X; penicillin M.I.C. 0.008 unit per ml.; (2) 7 out of 10 cultures over 29 days; group not A, C, or H; penicillin M.I.C. 0.06 unit per ml.; (3) 5 out of 9 cultures over 24 days; group not A, C, or H; (penicillin sensitivity not recorded). In 5 patients treated by penicillin and tonsillectomy throat cultures were invariably negative after treatment, and at operation the tonsillar fossae and tonsils themselves were also sterile on culture. From 28 to 43 of these cultures were taken per patient over postoperative periods varying from 112 to 180 days. In these cases the interval between initial penicillin treatment and operation varied from 125 to 185 days.

Antistreptolysin O titres are charted in 3 cases (2 of which received penicillin) over periods varying from 150 to 360 days. There appears to have been no correlation between titre and positive throat cultures or between titre and penicillin treatment during these periods. Two pairs of cases are described in which a carrier of *Strep. haemolyticus* infected a non-carrier; in one instance the second child developed an uncomplicated streptococcal sore throat, responding rapidly to penicillin treatment. In the other instance the second child showed a rise in antistreptolysin O titre and an acute exacerbation of rheumatic fever beginning 2 weeks after the first positive throat culture, though there was no fever or clinical evidence of "streptococcal" illness. This patient did not receive penicillin.

A smaller and less complete investigation is also reported. Of 6 streptococcal carriers found in the Wellesley Convalescent Home, 5 were rendered free from streptococci by ten daily injections of 150,000 units of penicillin in beeswax and peanut-oil. [It would probably have been wise to culture the nasal passages as well as the throat; the nasal-carrier rate has been said to be higher than the throat-carrier rate.] G. I. C. Ingram.

**Rheumatic Fever.** ALLEN, R. M., and LAMB, B. J. (1948). *Nebraska St. Med. J.*, 33, 124.

**Genesis of Rheumatic Fever.** SPINK, W. W. (1947). *Minn. med.*, 31, 267.

**Michigan's Rheumatic Fever Program.** ANGOVE, P. C. (1948). *J. Mich. med. Soc.*, 47, 281.

**Present-day Concepts of Rheumatic Fever.** MARTIN, A. T. (1948). *Ohio St. med. J.*, 44, 265.

**Modern Concepts of Rheumatic Fever.** MARTIN, A. T. (1947). *Mississippi Dr.*, 25, 231.

**Environmental Care for Children with Rheumatic Fever.** JACKSON, R. L. (1948). *J. Iowa med. Soc.*, 38, 45.

**Scarlatinal Rheumatism.** (Le rhumatisme scarlatin.) TRAISSAC, F. J., and MONTEYROL, — (1948). *Paris méd.*, 38, 153.

**Rheumatic Pneumonia.** (Polmonite reumatica.) TOSCANO, T. (1948). *Med. ital., Milano*, 28, 29.



## Chronic Articular Rheumatism

## (Rheumatoid Arthritis)

**Gold Therapy in Rheumatoid Arthritis.** BROWNING, J. S., RICE, R. M., LEE, W. V., and BAKER, L. M. (1947). *New Engl. J. Med.*, 237, 428.

The results of 6 years' experience in the treatment of rheumatoid arthritis by chrysotherapy are summarized. A course consisted of 1 g. in 100 mg. weekly doses of either myochrysine or gold acetyl cystein, each substance containing approximately 50% gold. During the last 4 years the dose has been reduced to 50 mg. weekly, although the total amount has remained the same. A maintenance dose of 25 mg. every 2 weeks has been employed after the "course" is finished. The clinical state was assessed on a modification of the [valuable] numerical index system of Bayles and Hall (*New Engl. J. Med.*, 1943, 228, 418). A fall of 2 points in this index was considered significant evidence of a clinical improvement. Records of 47 patients were examined, 34 being female and 13 male. All had had more than 100 mg. of gold, and record extended for from 18 months to 6 years; 18 cases had a history of less than 2 years' duration.

Results showed generally a 23% improvement (11 cases), with the greater improvement in cases of short duration and in those having the lesser total quantity of gold. Five patients died within the period, but in only 1 case do the authors directly attribute death to the gold; 62% of the entire group had toxic manifestations—skin irritation, exfoliative dermatitis, purpura, neutropenia, and renal irritation. Results correspond with those of Short and others (*New Engl. J. Med.*, 1946, 235, 362).

[The "courses" appear to have been given by rule, without attention to the dictum of Levinthal and Logan that "in each case an attempt must be made to treat each patient as a separate and distinct problem". The number of cases is small, and percentage figures are of false value. The results are comparatively poor and toxic effects extensive, due probably to the lack of a method of selection. One must not overlook the fact that "in addition, acetylsalicylic acid has been used freely to control pain, and application of heat to affected joints has been a daily routine with the majority of patients".]

Harry Coke.

**Combined Antigens in the Treatment of Rheumatoid Arthritis.** WARTER, P. J., DONIO, D. A., and HOROSCHAK, S. (1947). *J. med. Soc. N.J.*, 44, 441.

The authors consider that even though the streptococcus may not be the cause of rheumatoid arthritis its toxins and toxic products may be considered as contributing factors. [The work of Wallis (*Amer. J. med. Sci.*, 1946, 212, 713), who considers the bacterial theory, and more specifically the haemolytic streptococcal theory, of the origin of rheumatoid arthritis to be based on insecure foundations, has been ignored.] As a supplement to treatment a combined antigen of "*Staphylococcus aureus* 1,000 M per ml., *Staphylococcus toxoid* 500 M.N.D. per ml., *Streptococcus* (haemolytic, non-haemolytic, and *viridans*) 2,000 M per ml., and *Streptococcus* toxin (tannic-acid precipitated) 1,000 S.T.D. per ml." was used. The combined antigen was given intramuscularly at weekly intervals for at least 16 weeks, starting with 0.1 ml. and increasing by 0.1 ml. to a maximum of 1 ml. The injections were then given at 2-weekly intervals and later at monthly intervals if progress was

satisfactory. Occasional rest periods of several months were allowed to patients showing appreciable clinical improvement.

Ninety patients were observed for periods of 2, 3, and 4 years. The New York Rheumatism Association's recommendations for assessing improvement in rheumatoid arthritis were followed and the response to treatment was assessed as—Grade 1: complete remission; Grade 2: major improvement; Grade 3: minor improvement; Grade 4: no improvement. The results were:

Years observed	Grade 1		Grade 2		Grade 3		Grade 4	
	F	M	F	M	F	M	F	M
4	3	2	6	1	2	0	3	0
3	6	4	8	5	3	2	0	1
2	10	4	12	3	6	3	4	2
Total	29		35		16		10	

The authors conclude that the combined antigen used by them should be included in the therapeutic regimen for rheumatoid arthritis. [The investigation is uncontrolled, details of other forms of treatment used are not given, and the possibility of any beneficial results being due to a protein-shock effect is not considered.]

T. G. Reah.

**The Optimum Rest-exercise Balance in the Treatment of Rheumatoid Arthritis.** PIERSOL, G. M., and HOLANDER, J. L. (1947). *Arch. phys. Med.*, 28, 500.

The authors consider that careful movement of an arthritic joint may be carried out at any time except when it produces excruciating pain. They define the optimum exercise-rest balance as the ratio between the maximum amount of activity the patient can perform without excessive fatigue or residual increase of pain or muscle spasm and the minimum period of rest needed before the activity can be resumed in the same degree. Thus, if a patient exercises for 5 minutes and needs an hour's rest interval, his ratio is 1 to 12 and his periods of rest and activity should be repeated at these intervals. If the degree of activity prescribed remains constant for the patient, then the day-to-day increase in the ratio can be used as a quantitative index of improvement. Increasing pain, spasm, and fatigue indicate that exercise should be reduced. Ambulatory exercises should vary inversely with the activity of the disease in the weight-bearing joints; when weight-bearing is altogether contraindicated the exercises should be given in bed. Mild exertion many times a day is preferable to exertion to the extreme limit of endurance once or twice.

B. S. P. Gurney.

**Blood Transfusions in the Treatment of Rheumatoid Arthritis.** [In English.] APPELQVIST, O., and HOLSTI, Ö. (1947). *Schweiz. med. Wschr.*, 77, 977.

Twenty-four cases of chronic rheumatoid arthritis were treated by blood transfusion. The normal dose was 300 ml. and the average number of transfusions five. In grouping the blood no account was taken of the Rh factor, though the importance of this, especially in the case of young women, is pointed out. A febrile reaction followed 50% of the transfusions, and these reactions tended to precede an immediate improvement in the clinical condition. The results were favourable, though



rarely dramatic. Improvement in the clinical condition was more marked than a relatively small reduction in the erythrocyte sedimentation rate would indicate. The authors make a plea for the use of blood transfusion in preference to gold. H. F. Turney.

**The Heart in Rheumatoid Arthritis. Clinical, Radiological, and Electrocardiographic Study of 50 Cases.** (O coração na artrite reumatóide. Estudos clínico, radiológico e electrocardiográfico sobre 50 casos.) LUCCHESI, O., LUCCHESI, M., and KNEESE DE MELO, H. (1947). *Hospital, Rio de J.*, 32, 699.

This article deals with the findings in 50 private patients with rheumatoid arthritis—37 women and 13 men between the ages of 22 and 66; the duration of the arthritis varied from 1 month to 41 years. Subcutaneous nodules were present in 14 patients. On clinical examination, 26 hearts appeared to be normal, the rest having apical and basal systolic murmurs of the functional type. Radiological findings were normal in 80%; the rest had left ventricular hypertrophy due to hypertension. In no case could any signs suggestive of "rheumatic heart disease" be found. Electrocardiographically, 74% were normal, the remainder showed changes due to degenerative phenomena. Of the 14 patients with subcutaneous nodules, 7 were completely normal and 7 had changes associated with hypertension. The authors conclude that in rheumatoid arthritis there is no specific cardiac pathology, that subcutaneous nodules are of no prognostic value (contrast rheumatic fever), and that rheumatoid arthritis and acute rheumatism are distinct clinical entities. [This is a well-balanced article and merits attention.] Paul B. Woolley.

**Granulocytopenic and Lymphocytopenic Hypersplenism Associated with Atrophic Arthritis.** [In English.] LEVY, H. (1947). *Acta med. scand.*, 129, 203.

In Felty's syndrome the splenomegaly and leucopenia are associated with arthritis. It is impossible to say whether the splenomegaly and leucopenia are a sequel to the arthritis, or whether the splenomegaly is the primary lesion. A chance combination of two diseases would appear to be unlikely. The theory of a chronic infection involving both spleen and joints has been held by many, but the author throws doubt on this, especially as in some cases splenectomy improves the arthritis and causes the disappearance of the leucopenia. How the spleen causes the leucocytes to disappear is also doubtful. Phagocytosis or a hormonal influence on the bone marrow are both possibilities.

A case of atrophic arthritis and leucopenic splenomegaly is reported in a woman of 69. The arthritis had been present for 13 years. The lower border of the spleen was 5 in. below the costal margin, and the liver  $1\frac{1}{2}$  in. below. The erythrocyte count on admission was 3.9 millions per c.mm., and the white cells numbered 1,000 (62% lymphocytes). At one point the leucocyte count fell to 500. A sternal puncture showed active erythropoiesis and especially myelopoiesis. Splenectomy was not performed in view of the patient's age and the absence of pain. G. W. Whittall.

**Prothrombin Time in Rheumatoid Arthritis.** GRANIRER, L. W. (1948). *N.Y. St. J. Med.*, 48, 291.

Treatment of 15 patients with rheumatoid arthritis for a year with gold salts and liver did not change the prothrombin time. S. S. B. Gilder.

**Intoxication by Gold During the Treatment of Rheumatism: Its Cure by Bal.** (Goudintoxicatie bij reumatherapie en haar genezing met Bal.) URLINGS, D. A. J. M., and AMERICA, A. F. (1948). *Ned. Tijdschr. Geneesk.*, 92, 1072.

**The Relations of the Vascular Apparatus to Rheumatoid Arthritis.** WALLIS, A. D. (1948). *Sth. med. J.*, Nashville, 41, 362.

**Treatment of Rheumatoid Arthritis.** TEGNER, W. S. (1948). *Lancet*, 1, 469.

**Treatment of Rheumatoid Arthritis.** PINCKNEY, M. M. (1948). *Va med. Mon.*, 75, 131.

### (Osteo-arthritis)

**The Surgical Treatment of Chronic Arthritis of the Hip.** (A propos du traitement chirurgical des arthrites chroniques de la hanche.) TREVES, A. (1947). *Rev. Rhum.*, 14, 374.

The results of neurotomy, arthrodesis, and arthroplasty in the treatment of chronic arthritis of the hip are not good. Arthroplasty is a severe operation with an appreciable mortality and is suitable only for young subjects in good condition, while shortening may be increased, adduction not improved, and stiffness aggravated. Arthrodesis does not relieve pain or shortening and results in a permanent infirmity, and there is always the possibility of involvement of the other hip. After arthroplasty and arthrodesis, failure is irremediable. The author prefers to carry out a high subtrochanteric osteotomy at the level of the base of the greater trochanter, slightly obliquely, downwards and inwards to just below the level of the insertion of the ilio-psoas to the lesser trochanter. The adduction, external rotation, and flexion can thus be corrected. By a slight modification of the operation an intertrochanteric osteotomy may be performed with success. The author maintains that osteotomy is a simple and safe operation, and gives constantly good results. Patients are in plaster for 7 weeks after operation and there have been no complications. The effect of the higher osteotomy is probably not entirely mechanical; it may affect the intra-articular circulation as does drilling, but in a more intense and lasting manner. Further operative intervention is also possible after osteotomy. [The paper is not supported by statistics, and the good results claimed may be due to the immobilization in plaster, while the Smith-Petersen cup arthroplasty is not sufficiently considered.] T. G. Reah.

**A Report of Six Cases of Coxa Magna Following Synovitis of the Hip Joint.** MCMURRAY, B. (1947). *Brit. J. Radiol.*, 20, 477.

The author points out that any infection about the hip-joint may stimulate the growth of the head of the femur, producing x-ray changes which may later lead to an osteo-arthritic condition of the head of the femur due to disproportion between the head and the acetabulum. In the 6 cases described there was a history of subacute or acute infection of sufficient length to cause 5 weeks' invalidism before the onset of synovitis, which generally followed some minor trauma. All the patients were in the growing age, from 1 to 11 years. Examination showed signs of inflammation of the hip-joint, glandular

enlargement, and evidence of synovitis of the hip; there was an evening rise in temperature. Radiographs revealed decalcification, and this persisted for periods up to 1 year. Enlargement of the head of the femur began from 6 to 10 months after the onset of synovitis.

This short paper is interesting in that it throws light on the condition of coxa magna and explains certain cases of idiopathic arthritis, which occurs at a later date.

K. H. Pridie.

**Chronic Degenerative Arthritis of Shoulder following Acute Gonococcal Arthritis.** (Arthrite chronique dégénérative de l'épaule séquelle d'une arthrite gonococcique aigue.) FRANÇON, F. (1948). *Rev. Rhum.*, 15, 15.

#### (Spondylitis)

**Spondylitis due to *Salmonella paratyphi* B.** (Spondylitis framkalt av *Salmonella paratyphi* B. En oversikt og et tilfelle.) ANCHERSEN, P. (1947). *Nord. Med.*, 36, 2019.

The first case of spondylitis (or other bone complication) due to paratyphoid B infection in Norway is reported. The patient, a man of 50, had a paratyphoid B infection at the age of 17 (in 1915); while he was recovering from this he had fever and severe pain in his right thigh and hip. After 5 days this cleared up. At the age of 35 he had a right psoas abscess, and radiographs revealed bone destruction of long standing in the third and fourth lumbar vertebrae, the bodies of which had become fused. The condition was considered to be tuberculous. The abscess burst spontaneously and continued to discharge for 7 years. After 6 years' clinical remission he developed a left lumbar abscess in which *Salmonella paratyphi* B was demonstrated. Radiographs showed no change since 1933. The author considers that the pain in the hip in 1915 was probably due to "paratyphoid spine", but that the later condition was really a chronic paratyphoid osteomyelitis. The treatment of this case was by surgical incision and drainage. A few weeks after operation there was a small fistula with scanty secretion.

A. M. M. Wilson.

#### (Miscellaneous)

**Retroposition of Vertebrae as an Early Sign of Tuberculous Spondylitis of the Lumbar Spine.** [In English.] HAGELSTAM, L. (1947). *Acta orthopaed. scand.*, 17, 31.

The significance of retroposition of a lumbar vertebra in radiographs of the lumbar spine is discussed. Seven cases are described in which such retroposition was seen at a relatively early stage in infection of the spine; the condition was tuberculous in 6 and probably pyogenic in one. The retroposition is associated with reduction in disc space and indicates disease of the disc. When the disc has been destroyed the retroposition disappears or is considerably reduced. The radiographs of the lumbar spine in flexion and extension from an early tuberculous case are shown to illustrate that the retroposition may disappear in flexion, that it is, in fact, simply evidence of the instability of the spine associated with any disc disease, and does not differ from that seen in simple disc degeneration and prolapse, as described earlier by Severin and Knutsson. The value of this early sign of spinal disease is emphasized. It may in some cases be more easy to detect than narrowing of the disc space,

which may be attributed to the obliquity of incidence of the x-rays at the border of a film.

J. Agerholm-Christensen.

**Tuberculosis and Rheumatism.** (Tuberculose et rhumatisme.) MARTIN, E. (1947). *Arch. Rhum.*, 7, 89.

At the beginning of the century Poncet came to regard many forms of "rheumatic disease" as manifestations of tuberculous infection. He wrote: "In the presence of rheumatism, what one must first prove is that it is not tuberculous."

The present author thinks that French clinicians are too ready to diagnose "Poncet's rheumatism", but, on the other hand that Anglo-Saxon workers are wrong in denying the occasional correlation of rheumatism and tuberculous infection. Several cases are described and reported as instances of the type of rheumatism which is probably tuberculous in nature.

(1) A patient, aged 20, suffered from an acute polyarticular rheumatism, at first vagrant in character, but later showing permanent joint changes. Pleurisy and other tuberculous lesions developed, and death followed from tuberculous meningitis. Necropsy revealed widespread tuberculous lesions, including tubercles with typical giant cells in some of the foot joints.

(2) A patient, aged 30, developed an acute sore throat with enlarged tonsils and acute articular rheumatism. One tonsil after removal showed tuberculous infection, with caseation and typical giant cells. The joint reactions abated after the tonsils were removed. This observation suggests that a tuberculous tonsil can cause acute polyarticular rheumatism.

(3) The patient, a woman aged 31, had suffered for 5 years from joint reactions with the features of allergic polyarthritis. There was a history of pleurisy at the age of 13 and of haemoptysis at 19. The patient died, and at necropsy tuberculous lesions were seen in the lungs. No typical lesions could be found in the joints, but there were perivascular collections of lymphocytes and plasma cells. Two tubercle bacilli were, however, seen in a macrophage, and infection of the synovial membrane was demonstrated by guinea-pig inoculation.

(4) A woman died at the age of 50 with chronic polyarthritis and pulmonary tuberculosis. The arthritis had evolved slowly over a period of 7 years, and clinically was a progressive polyarthritis of the rheumatoid type. Throughout its evolution tuberculosis was present, at first alone, later dominating the clinical picture. At necropsy several extra-articular cold abscesses were found; the joints of the lower limb and the wrists were ankylosed; there was a tuberculous infection of the bone close to the right knee-joint.

[The original should be consulted for full description of these cases. They would seem to be instances of the several types of joint reaction which may result from tuberculous infection; and they may serve to indicate the urgent need for a definition of "rheumatism".]

Kenneth Stone.

**The Shoulder-Hand Syndrome. Associated Painful Homolateral Disability of the Shoulder and Hand with Swelling and Atrophy of the Hand.** STEINBROCKER, O. (1947). *Amer. J. Med.*, 3, 402.

The author describes 6 cases (5 females, 1 male) in which a painful disability of the shoulder was combined with swelling of the homolateral hand, followed in 5 by trophic changes. The onset was either acute or insidious, and the shoulder and hand symptoms might arise simultaneously or either might appear first. The



initial swelling of the hand showed little or no pitting, and the colour might be pink, pale, or cyanotic. There was widespread tenderness round the shoulder and over the hand. After 3 to 6 months, pain lessened and the swelling disappeared, but stiffness and flexion deformity of the fingers, especially on the ulnar side, tended to appear, accompanied by progressive osteoporosis of the bones of the hand and shoulder. In the mildest case recovery was complete in 10 months, but in others the duration varied between 1½ and 7 years, and in one case flexion deformities of the fingers were still present after 7 years.

The syndrome seems to be a definite clinical entity but the aetiology is obscure. There was a history of mild trauma in only 1 case, and no patient had a history of preceding infection. Five were under great emotional strain [the possibility of an hysterical basis is not discussed]. In 2, osteo-arthritis of the cervical spine was demonstrated radiologically. A rather similar condition has been described as a rare sequel to cardiac infarction, but there were no symptoms or signs suggesting coronary disease in these patients, and the electrocardiogram was normal in the 4 cases in which it was available. The erythrocyte sedimentation rate was normal in 5 patients and raised in 1.

[The author attributes the condition to a "disturbed neuro-vascular mechanism", but unfortunately no information is given on sensation, reflexes, arterial and venous pressures, reactive hyperaemia responses, skin temperatures, or any other tests of nervous or vascular function in the affected limbs.]

A. R. Kelsall.

**The Prolonged Therapeutic Action of Intracaine in Painful Musculoskeletal Disorders.** BETTMANN, E. H. (1947). *N.Y. St. J. Med.*, 47, 2193.

The author finds that "intracaine" ( $\beta$ -diethylaminoethyl-*p*-ethoxy benzoate) in oil, in 2% or 5% concentration, has a prolonged analgesic action with almost complete absence of local toxicity. From the clinical studies which he records it would appear to be of great value in the treatment of several painful musculo-skeletal disorders. It is considered to be especially valuable in the treatment of low back pain, certain fractures, subacromial bursitis, contusions, muscle tears, epicondylitis, and certain ligamentous injuries. In the treatment of arthritis parietal-articular injection was given; it was found that intra-articular injection caused increased pain and effusion.

Kenneth Stone.

**Idiopathic Scoliosis. A Method of Correction.** THOMAS, G. E. (1947). *J. Bone Jt. Surg.*, 29, 907.

In the treatment of idiopathic scoliosis the author favours: (1) recumbency on a Thomas spinal frame with head-piece for 3 to 4 days; (2) continuous traction by skin extensions to the foot-pieces of the frame plus 10 lb. weight traction on a Sayre halter (this is applied after 3 to 4 days, the head of the bed being raised 2 ft.); (3) lateral pressure, started 2 days later, by screw-pressure pads applied to the horizontal bars of the Thomas frame. One pad is applied to the thorax opposite the point of greatest curve. The two others are on the opposite side, one against the pelvis and the other against the chest-wall at the upper extremity of the curve, usually near the axilla. The weight is increased by about 7 lb. daily up to 30 lb. for an adult. The screws are tightened twice daily and should never cause discomfort. Screws and weights are released once daily for skin toilet. The method has failed in a patient

with a curvature which was too high in the thoracic spine and in 2 patients with curvatures of grotesque severity. It is also not advised for lumbar curvature. In 12 suitable cases maximal correction was obtained within 8 weeks. The amount of lateral correction obtained bore no constant relation to the degree of rotation present.

D. L. Griffiths.

**Experience and Results from Mobilizing Plastic Operations in Four Cases of Osseous Ankylosis of the Knee.** [In English.] STÖREN, H. (1947). *Acta. orthopaed. scand.*, 17, 146.

Four cases of arthroplasty on knees with bony ankylosis are described. The ankylosed joint was exposed by Payr's incision, the bone ends were separated and trimmed into semicylindrical shape, and a strip of fascia lata was placed over each surface and carefully sutured down. After-treatment consisted of extension for 4 to 5 weeks, followed by controlled movement and weight-bearing in about 6 weeks. One patient had to be re-operated upon 2½ years after the first operation, and the result was satisfactory. The remaining 3 patients had good stability and movement. One had pain but was able to work. Two cases had been under observation for only 1½ and 2 years. In the case re-operated upon it was found that the two layers of fascia lata had fused with the capsule. The bone ends were quite smooth and covered with a layer of newly formed fibrocartilage.

J. W. S. Lindahl.

**A Technique for Arthroplasty of the Elbow Joint.** ARMSTRONG, A. C. (1947). *Med. J. Aust.*, 2, 716.

This paper describes an operation for arthroplasty of the elbow-joint which has been carried out with success on 2 soldiers in whom ankylosis had resulted from war wounds. They obtained 60% of normal movement, with no instability and with good power.

E. L. Willis.

## Sciatica

**The Role of Spinal Fusion in Arthrogenic Sciatica: A Review of 52 Cases.** WEST, E. F. (1947). *Med. J. Aust.*, 2, 711.

The author reviews 52 cases of sciatica due to changes in the posterior intervertebral joints of the lower lumbar spine treated by spinal fusion. He believes this type of sciatica to be due to irritation of one or more nerve roots in close proximity with the arthritic joints. The primary cause of the arthritis is degeneration of the corresponding intervertebral disc, allowing the vertebral bodies to approximate and thus causing malalignment of the apophyseal articulations. In 13 cases the condition was associated with spondylolisthesis. The condition occurs more commonly in middle age or later, the average age in this series being 42. Chronic low back pain and limitation of movement for some years are followed by sciatic pain. Radiologically the disc space is much diminished and changes may be demonstrated in the apophyseal joints, particularly in oblique views. In many cases it may be difficult to exclude disc herniation.

A period of conservative treatment with immobilization in a hip spica was tried in all cases. In 11 cases laminectomy was performed; in 6 of these fusion was carried out at the same operation and in the other 5 at



a second operation. In 2 cases a disc protrusion was found. The author prefers extra-articular fusion from the second lumbar vertebra to the sacrum, because he has known arthritic changes above the graft to follow a more limited fusion. He prefers curved tibial grafts reinforced by spongy bone from the tibia. The series includes 42 tibial, 8 iliac, and 2 combined grafts. Of the 52 patients, 37 have been followed up for more than 8 months, 26 of these have obtained complete and lasting relief. Of 7 patients in whom fair results were obtained, 6 still have some back pain and mild sciatica, and 1 has persistent coccydynia. One patient died, in 2 cases fusion has failed, and 1 patient complains of pain at the operation site.

E. L. Willis.

**Primary Isolated Degenerative Chondrodystrophic Changes in Intervertebral Disks.** (Le alterazioni condrodistrofiche degenerative primitive isolate della fibrocartilagine intervertebrale. Considerazioni sui loro rapporti con le ernie del disco.) GARDELLA, G. (1947). *Ann. Radiol. diagnost.*, 19, 265.

Five cases of primary degeneration of the fibrocartilage of the intervertebral disc are described. The radiographic differential diagnosis between this condition and affections of the disc resulting from trauma or infective diseases is discussed. The author is inclined to attribute the degeneration of the disc to repeated minute traumata ("microtraumata"), and considers that there is a close relation between the spontaneous prolapse of the disc and its fibrocartilaginous degeneration.

A. Orley.

**Sensory Disturbances occurring in Sciatica due to Intervertebral Disc Protrusions: Some Observations on the Fifth Lumbar and First Sacral Dermatomes.** FALCONER, M. A., GLASGOW, G. L., and COLE, D. S. (1947). *J. Neurol., Neurosurg., Psychiat.*, 10, 72.

In contrast to the generally accepted teaching, the authors have found that by careful sensory testing in cases of protrusion of the intervertebral disc they were able to outline a pattern of sensory change which extended from buttock to toes, even when only one root was involved. Further observations led them to believe that the area of loss represents a dermatome; this indicates that the classical descriptions of the dermatomes by Head, Dejerine, and Foerster are faulty.

The observations were made on 50 consecutive patients suffering from sciatica. Sensory disturbances were more easily detected with painful stimuli. Hypoalgesic areas were found in 33 patients. Each pattern was characteristic of a particular nerve root. The fifth lumbar root was associated with a strip 3 to 6 in. (7.5 to 15 cm.) wide stretching from the foot to the lumbar region. On the foot this area occupied the dorsum and middle three toes and involved a wedge-shaped area of the sole. Above, it included the lateral surface of the leg; on the thigh it passed in a gradual spiral on to the posterior surface and then crossed the buttock to end in the lumbar region at the midline. The area associated with the first sacral root resembled this, but lay more laterally in the foot and leg and at a lower level in the lumbar region. By anaesthetizing the nerve root, for which an ingenious method is described, the authors were able to reproduce this sensory loss in the sound leg of their patients.

[It is notoriously difficult to be certain where minimal changes of sensation are concerned, and there may be some difficulty in accepting these findings *in toto*.]

N. S. Alcock.

**Backward Displacement of Fifth Lumbar Vertebra in Degenerative Disc Disease. The Significance of the Difference in Anteroposterior Diameters of the Fifth Lumbar and First Sacral Vertebrae.** FLETCHER, G. H. (1947). *J. Bone Jt. Surg.*, 29, 1019.

Of 600 patients complaining of backache, 10% were found to have backward displacement of the fifth lumbar vertebra on the first sacral vertebra. Lateral radiographs [which would have to be far better than those usually obtainable in Britain] are used to measure the displacement. The points of measurement are vague because of the presence of osteophytes, but there is an average difference in diameter of 3 mm. between the fifth lumbar and first sacral vertebrae. This condition of backward displacement is due to a degeneration of the intervening disc and facets in a frontal plane. These patients have backache and not sciatica, and the author states that removal of the disc is not indicated but that treatment should be by fixation.

K. H. Pridie.

**Prognosis in Medically Treated Sciatica. (A Follow-up Investigation of 256 Patients.)** [In English.] YTREHUS, O. (1947). *Acta med. scand.*, 128, 452.

The author reviews 256 patients (151 men and 105 women) who suffered from sciatica in the period from 1938 to 1944. All cases of "symptomatic sciatica" are excluded, but those with radiological evidence of spondylitis deformans and osteochondrosis are included. In addition to pain, a positive Lasègue's sign was present in all cases. Most patients were between the ages of 20 and 50 years, mostly in the age-group 30 to 39; the period of observation varied from 2 to 8 years, with an average of 4.7. Over a third of the males were engaged in laborious occupations. In 118 cases the sciatica was on the right side, in 110 on the left and in 28 on both sides or with a history of previous sciatica on the other side. A complete neurological examination was not made in all cases. A radiological examination of the lumbar spine was made in 248 cases with air-myelograph in 8 cases; and changes, usually of spondylitis deformans or osteochondrosis, were noted in 44.3%. Spondylolisthesis was present once, and sacralization of the fifth lumbar vertebra in 3 cases. Lumbar puncture was performed in 91 cases with no significant findings. The patients were divided into three groups according to the prominence of Lasègue's sign: (1) sign positive at 60 degrees or more; (2) sign positive at from 60 to 30 degrees; (3) sign positive at less than 30 degrees.

Patients were confined to bed until free from pain when at rest and until Lasègue's sign was not positive until 60 degrees was attained. Local heat and analgesics of the salicylate group were given, with massage when the patients were free from pain. X-ray treatment was given in 21 cases of spondylitis deformans, but injection treatment and braces were used in only 2 cases. The average time spent in hospital was 32.2 days, with averages of 22.5 days for group 1, 33 days for group 2, and 57.4 days for group 3. On discharge from hospital 46.7% of the patients were free from symptoms and the others were in most cases considerably relieved.

Replies to an inquiry form were received from 220 patients, and 140 were re-examined. Seven patients were operated on and are excluded from the final review. Of the 213 patients, 122 were men and 91 women. The results are summarized in the table.

The condition recurred in about 30% and in 10.8% necessitated readmission to hospital. Most relapses were in patients who performed heavy work and in those

	Fully capable of work without pain	Fully capable of work with pain	Reduced ability to work	Reduced ability to work owing to complicating diseases
Men ..	42	51	26	3
Women ..	30	29	30	2
Total ..	72	80	56	5
% ..	33.8	37.0	26.8	2.4

with severe sciatica; frequency of relapse also rose with an increasing period of observation. The average period of disablement for work after recurrence was 65 days. In all the cases reviewed the average duration of incapacity for work before, during, and after admission to hospital was 92.3 days. Changes in the ankle-jerk are of no prognostic significance, but with a positive Lasègue's sign of less than 30 degrees the disease generally had a longer duration and an increased tendency to relapse.

Indications for operation are persistent intense pain and the presence of serious neurological findings. Conservative treatment should first be tried for 3 months; if after this period no satisfactory progress has been made, operation should be considered.

T. G. Reah.

**Sciatica, Especially the Prognosis by Conservative Treatment.** [In English.] BOYSEN, G. (1947). *Acta med. scand.*, 128, 473.

During the period from Jan. 1, 1938, to July 1, 1944, 431 patients (220 men and 221 women) were diagnosed as suffering from sciatica. The right and left sides were equally affected, and in 60 patients the pain was bilateral. The patients were mainly between 26 and 50 years, mostly in the 36 to 40 age group. The average stay in hospital was 41 days. A lumbar puncture was performed on 169 patients, with abnormal findings in 36. Of 282 patients examined by a neurologist, signs were found in 153, usually loss of sensibility over L5 or S1 segments or alterations in the ankle-jerk. Radiologically the lumbar spine, pelvis, and hip-joints were normal in 27.5% of the 338 patients examined, and in those patients with positive findings the radiological changes were often difficult to relate to the sciatica. Myelography was performed 38 times—24 times with "lipiodol" and 14 with air—and in 19 patients a prolapsed intervertebral disc was demonstrated.

An inquiry form identical with that sent out by Ytrehus (see above Abstract) was used, and replies were received from 277 patients, of whom 183 were re-examined. Operations had been performed on 16 patients and 1 had died, leaving 260 cases for final review. Of these, 225 were completely fit for work, 30 fit for light work, and 5 unfit for work, but in only 2 of these 5 patients was the sciatica alone the cause of the total incapacity. Symptoms of sciatica persisted in 205 patients. There were 83 relapses, with an equal incidence in men and women and a higher incidence in the younger age group. No criteria were found which would assist in detecting those cases likely to relapse. Of the 16 patients treated surgically, 10 made good recovery, 4 relapsed, and 2 were observed for too short a period to assess the result.

Treatment consisted of rest, analgesics, heat, and massage. Patients suffering from spondylosis received x-ray treatment, and in recent years corsets have been

used, first of plaster-of-Paris and later of paper. Persistent pain, neurological changes, and reduction of capacity for work are indications for operation.

J. G. Reah.

**A New Contribution to the Study of "Surgical" Sciatica.** (Nouvelle contribution à l'étude de la sciatique chirurgicale.) ALAJOUANINE, T., and THUREL, R. (1947). *Sem. Hôp., Paris*, 23, 2794.

This paper contains mainly statistical details based on 500 operations for sciatica. In only 5 cases was the whole sciatic nerve affected—in 3 a pelvic tumour was found, the fourth was due to an injection into the nerve, and the fifth was caused "by the pressure of the child's head during delivery". In 99% of all cases only one root of the nerve was affected; in 83% of these a prolapsed intervertebral disc was found at operation. In 12% of the cases no cause was found, but the authors believe that insufficient experience and lack of exact x-ray examination with "lipiodol" have prevented their finding a herniated disc. The remaining cases of "surgical sciatica" were made up of tumours of the cauda equina, metastatic cancer of the spine, and tuberculous infection of the epidural tissues or meninges.

Of all patients 70% were men, 30% women; 4% were below 20, 19% between 20 and 30, 35% between 30 and 40, 30% between 40 and 50, 10% between 50 and 60, 2% over 60. The prolapse was found at the lumbosacral level in 40% of the cases, at the fourth lumbar disc in 55%, at the third lumbar disc in 2%. Bilateral hernias were found in 6% of all cases. F. K. Kessel.

**The Origin of Pain in Sacralization of the Lumbar Vertebrae; Importance of Changes in the Lumbosacral Disk.** (Origine des douleurs dans la sacralisation douloureuse importance des altérations du disque charnière.) DE SÈZE, S., and SALOFF, J. (1947). *Rev. Rhum.*, 14, 368.

**Sciatica.** (Ciaticas.) LOPEX ZAMORA, R. (1948). *Rev. argent. Reum.*, 12, 241.

## Gout

**A New Case of Gouty Rheumatism.** (Considération sur un nouveau cas de rhumatisme goutteux.) WEIL, M.-P., POILPRÉ, E., and DAUSSET, J. (1948). *Rev. Rhum.*, 15, 92.

**Gout and Gouty Arthritis.** TALBOTT, J. H. (1948). *N. Y. Med.*, 4, 17, 36.

**Three Cases of Phlebitis in Gout.** (Sur trois cas de phlébite goutteuse.) PELLET, C. (1948). *Rev. Rhum.*, 15, 95.

**Gout Complicated by Leukaemia. Intravenous Colchicine.** (Goutte compliquée de leucémie. Colchicine intraveineuse.) COSTE, F., GALMICHE, P., and SORS, C. (1948). *Rev. Rhum.*, 15, 89.

**Treatment of Gout.** (A propos du traitement de la goutte.) PAILLARD, H. (1948). *Rev. Rhum.*, 15, 88.

**The Problem of Gout.** (Le problème de la goutte.) WEIL, M.-P., and MONTALANT, P. (1948). *Rev. Rhum.*, 15, 65.



## General Articles

**Palindromic Rheumatism.** (Reumatismo palindrómico.) CALVO MELENDRO, J. (1947). *Rev. clin. esp.*, 25, 32.

An attempt is made to classify under the heading of benign articular rheumatism: (a) the affection described in 1941 by Hench and Rosenberg as palindromic rheumatism of unknown aetiology, and (b) the recurrent allergic arthritis. The common symptomatology comprises: rheumatic paroxysms, mostly mono-articular, recurring at various more or less regular intervals, without ever producing any permanent local or distal lesions or changes. Literature is abundantly quoted and a few personal cases are described. Attention is drawn to the fact that similar clinical pictures may be seen in tuberculosis, Malta fever, and focal infections. A. Lilker.

**Palindromic Rheumatism.** PERL, A. F. (1947). *Canad. med. Ass. J.*, 57, 382.

This rare affection was first noted by Hench in 1928. Dr. Perl's case, a girl of 18, first complained in November, 1945, of swelling and pain in her right wrist and both ankle joints—symptoms which she thought were caused by moving heavy containers at her job (wrist), and dancing (ankles). On examination slight swelling and tenderness of these joints was found, with discoloration and cutaneous eruptions on the front of her wrists; otherwise the findings, including temperature and sedimentation rate, were normal. The previous history was normal, though she and both parents were emotionally unstable, and her mother suffered from seasonal asthma. Rest soon relieved the symptoms, but they returned when she went back to work. Complete investigation revealed nothing unusual except for a relative lymphocytosis (48%). After two months in bed on the suspicion of rheumatic fever, she returned to her job, and the symptoms left her for six months. The author admits he is puzzled by a picture which most nearly resembles palindromic rheumatism, though the cutaneous eruptions suggest angioneural arthrosis; he recommends treatment with pyribenzamine or benadryl. He does not seem to lay much stress on the patient's unstable emotional background or upon the fact that the symptoms re-appeared several times soon after the patient had left her bed and returned to her job. T. E. C. Early.

**Periodic Disease. A Probable Syndrome Including Periodic Fever, Benign Paroxysmal Peritonitis, Cyclic Neutropenia and Intermittent Arthralgia.** REIMANN, H. A. (1948). *J. Amer. med. Ass.*, 136, 239.

Six cases of varied clinical syndromes are reported whose common feature is that, over a period of several years, they have recurred at remarkably regular intervals in attacks lasting several days. In 3 patients the main features were febrile episodes accompanied by abdominal and limb pains. In each the cycle was different; in the first, a woman of 49 with a history of 11 years' illness, the attacks lasted 5 to 7 days and recurred at intervals of 17 to 22 days unrelated to the menses; the only abnormal findings were a panleucopenia of 2,000 to 3,000 cells per c.mm. with a monocytosis of 7 to 21%, a raised erythrocyte sedimentation rate, and an increased globulin content of blood. The second patient, a man of 27, had headache, vomiting, general pains, and pyrexia in attacks lasting 2 days and separated by intervals of good health at first of 30 days shortening later to 7

days, the only abnormality being a slight leucocytosis (11,000). The third patient had a 3 years' history of attacks of pyrexia with abdominal pain, nausea, and occasional diarrhoea with a leucocytosis of 12,000 to 17,000, lasting for about 48 hours at intervals of 2 to 6 weeks. In none of these 3 cases was any infective factor unmasked, nor did the author discover any of the usual causes of recurrent pyrexia, which he lists as "Hodgkin's disease, non-suppurative relapsing panniculitis, undulant fever, relapsing fever, malaria, migraine, epilepsy, and certain psychoses". A fourth patient, a man of 20, suffered from cyclic neutropenia with increasing malaise, headache, sore throat, buccal ulceration, and cervical lymphadenitis; the attacks lasted for 5 to 7 days at intervals of 20 to 22 days. A fifth had an intermittent hydrarthrosis and the sixth a regular recurring myasthenia gravis. Several cases are quoted from the literature. The author concludes that there is as yet no satisfactory explanation for these medical curiosities, most of which recur independently of any known natural rhythmic functional fluctuations. Henry Cohen.

**Toxic Effects of Massive Doses of Calciferol in the Treatment of Chronic Rheumatism in Adults.** (Les accidents des fortes doses de calciferol dans le traitement des rhumatismes chroniques de l'adulte.) THIERS, H. (1947). *Rev. Rhum.*, 14, 304.

Calciferol was used in the treatment of certain chronic rheumatic disorders. The dose was 0.225 g. (15 ampoules each of 0.01 g.) during the first month, 0.15 g. (10 ampoules) or 0.12 g. (8 ampoules) during the second month, and 0.12 g. (8 ampoules) during the third month. No therapeutic effect is obtained with a dose of less than 0.12 g. (8 ampoules) a month.

Of 127 cases treated, toxic reactions occurred in 16 (7.3%). Clinical notes of these 16 cases are given. In none were the symptoms grave; in all they cleared up completely when administration of the vitamin was stopped. Usually reactions occurred about the end of the first month. Of those affected, 13 gave a history of some antecedent pathological process, and in 6 this was a disorder of the urinary tract. The most severe symptoms were seen in 6 cases of rheumatoid arthritis. Those attributed to hypervitaminosis were: (1) asthenia and wasting; (2) anorexia, thirst, and constipation; (3) albuminuria and pyuria. Other symptoms were liver pain and tenderness, epistaxis, partial deafness and tinnitus, and painful tongue.

It is essential that those who propose to treat chronic rheumatism with massive doses of calciferol should be familiar with these reactions, and that all patients should be warned of their possible occurrence. Absolute contraindications are: (1) prostatic hypertrophy; (2) a history of renal disorders such as calculus, urinary tract infections, albuminuria of pregnancy, and acute nephritis—even if they are apparently completely cured.

Kenneth Stone.

**Succinate-salicylate Therapy in Arthritis.** SZUCS, M. M. (1947). *Ohio St. med. J.*, 43, 1035.

The widespread systemic disturbance in some forms of arthritis is suggestive of a metabolic disorder, and this is supported by the evidence of altered tissue metabolism and respiration in this class of disease. There is in arthritis a diminished utilization of oxygen by the tissues. The toxicity of salicylates is probably due in part to their inhibitory action on tissue respiration and metabolism.



Adenylic acid and succinic acid are known to be normal tissue enzymes, and will correct the abnormal oxygen utilization. A consideration of these facts led the author to try the effect of calcium succinate in arthritis and rheumatic fever. Initially it was shown that the combined administration of calcium succinate and salicylates did not cause the expected fall in prothrombin, which occurs on administration of salicylates alone. Then 396 patients suffering from various forms of arthritis were given 45 gr. acetylsalicylic acid and 34 gr. calcium succinate daily for periods of 2 to 4 months. The results in various forms of arthritis were striking.

[The claims put forward are important, and the work needs careful repetition. It may be that tissue metabolism is one of the main features at fault, and the theoretical possibilities of the use of respiratory enzymes to correct such alterations opens a promising field of investigation.]

W. S. C. Copeman.

**Studies upon Spinal Cord Injuries. II. The Nature and Treatment of Pain.** DAVIS, L., and MARTIN, J. (1947). *Neurosurg.*, 4, 483.

Pain complicated a spinal injury in a group of 471 patients who came under the author's care at periods varying from days to years after the initial injury. Cord damage was cervical in 77, thoracic in 288, and due to the lumbar enlargement or cauda equina in 106. Pain was a prominent complaint in 126 (26%); 8 of these had cervical injuries, 73 thoracic injuries, and 45 lesions of the lumbar enlargement and below this level. Pain was thus commoner in injuries at lower levels.

Three types of pain may occur. Root pain is severe and unmistakable, and corresponds to the level of the vertebral damage. This was commonest in cauda equina lesions. Secondly, there is a diffuse continuous burning and tingling pain, not sharply localized and not confined to the distribution of a particular dorsal root. Every patient who suffered pain experienced these sensations. They were aggravated by climatic, psychological, and other factors. This pain appears early after the injury, increases to a maximum, and then diminishes, although it may persist for years. Thirdly, there is visceral pain. This consisted of a feeling of fullness in the abdomen associated with vesical distension or of vague abdominal discomfort after enemata. There might be associated feelings of nausea, sweating, flushing of the face, and headache. Such visceral pain occurred in 80% of the group of patients with pain.

The physiological mechanism in each type of pain is considered. That of root pain originating at the level of the lesion is obvious. The occurrence of visceral pain even with complete transection of the cord is understandable when it is remembered that afferent impulses from the viscera may run proximally in the splanchnic nerve and sympathetic chain for many segments before these impulses are transferred to the ascending sensory pathways in the cord through the posterior spinal roots.

The explanation of the diffuse burning pain occurring below a lesion regardless of its completeness or level is less obvious. Holmes and Foerster had suggested that it was due to irritation of ascending sensory tracts (in particular the spinothalamic) in the cord at the level of the lesion. The present authors suggest that the dilatation of the subarachnoid space at the level of the lesion would result in stimulation of the sensory tracts in the cord by every pressure variation in the space. This could result in pain and dysaesthesiae. Further, they

quote experimental evidence which suggests that afferent impulses from the lower limbs enter the cord after passing proximally through the sympathetic trunk for a considerable distance. They suggest that efferent impulses from uninhibited centres in the spinal cord below the level of the lesion may produce an H-like substance in the skin and muscles of the lower limbs. Peripheral stimuli normally unrecognized now give rise to afferent impulses that enter the spinal cord above the level of the lesion by way of afferent fibres related to the autonomic system. In this way the diffuse pains under consideration may arise.

[This paper presents a clear analysis of the pain which may complicate spinal injuries. The suggestion that afferent fibres from the limbs enter the cord after coursing through the sympathetic chain for a considerable distance is of much interest and is based on the experimental work of Kuntz as well as on clinical observation by the authors and others.]

J. E. A. O'Connell.

**Painful Disability of the Shoulder in Coronary Disease.** SCHOTT, A. (1947). *Proc. R. Soc. Med.*, 40, 733.

The author correlates coronary disease with a painful disability of one or both shoulders resembling scapulo-humeral peri-arthritis. Should this follow shortly after coronary occlusion it may not be recognized as a separate lesion and may therefore remain untreated, while if peri-arthritis is diagnosed independently the question arises whether it has any relation to coronary disease. Reference to previous papers quoted and his own experience leave little doubt in the author's mind that a definite relation does exist between coronary disease and peri-arthritis of the shoulder, although the mechanism is obscure. Six cases are briefly described. It is emphasized, however, that both conditions are common in patients over 40. In 138 cases of myocardial infarction—the largest series of cases so far investigated from this angle—Ernstene and Kinell (*Arch. int. Med.*, 1940, 66, 800) found 12% with scapulo-humeral peri-arthritis. The sex incidence in ordinary peri-arthritis is about equal, and the right shoulder is affected rather more often than the left (Dickson and Crosby, *J. Amer. med. Ass.*, 1932, 99, 2252). In a series of 68 cases in which peri-arthritis occurred together with coronary disease, there were nearly three times as many males as females, and in a series of 114 cases the left shoulder was affected almost twice as often as the right, thus confirming the observation of various authors that the shoulder affected tended to be on that side to which there had been radiation of the coronary pain.

Treatment, general and local, of the shoulder disability varies. The pain is not related to exertion or emotion, does not respond to trinitrin, and is stated to clear up in some cases after a few months and to persist in others for years.

The author suggests that more patients over the age of 40 with painful disabilities of the shoulder, especially of the left, without obvious cause should be examined for coronary disease in order to establish the frequency and nature of this relationship.

Donald Hall.

**The Plasma Viscosity in Rheumatic Diseases.** COWAN, I. C., and HARKNESS, J. (1947). *Brit. med. J.*, 2, 686.

The plasma viscosity was estimated in 320 cases of rheumatic diseases and 43 normal controls. Like the erythrocyte sedimentation rate (E.S.R.), it is a non-specific test, alterations of viscosity being dependent on the plasma proteins. Abnormal readings of the plasma

viscosity and E.S.R. are found in much the same type of case. It is suggested by the authors that the plasma viscosity is a more reliable guide to the patient's condition than is the E.S.R. Thus, clinically active cases of rheumatoid arthritis with a normal E.S.R. were found to have an abnormal plasma viscosity. In a number of cases clinical improvement was accompanied by a corresponding change in the plasma viscosity test though no such change was noted in the E.S.R. Unfortunately in the early stages of rheumatoid arthritis the plasma viscosity may still be within the range of normal; the E.S.R. has a similar disadvantage. The plasma viscosity test was normal in cases of fibrositis and in the upper range of normal in osteo-arthritis.

H. A. Burt.

**Inhibition by Sodium Salicylate of Cutaneous Diffusion of Hyaluronidase in Rheumatism.** (Inhibición por el salicilato de sodio de la difusión cutánea de la hialuronidasa en enfermos reumáticos.) GIL, J. R., and GUERRA, F. (1947). *Arch. Inst. cardiol. Méx.*, 17, 733.

In a previous paper the authors demonstrated the inhibition of cutaneous diffusion of hyaluronidase by sodium salicylate in healthy persons. In their present publication they deal with patients suffering from rheumatoid arthritis and rheumatic fever. Diffusion of the enzyme alone in the cutaneous tissue of rheumatic patients is more rapid and extensive than it is in normal persons. This difference may be due to an alteration in the connective tissue or to removal of a tissue barrier to fluid diffusion which may be a hyaluronic acid gel present in the interstitial tissue. Sodium salicylate has the same effect in rheumatic patients as in healthy persons—that is, it diminishes the spreading activity of hyaluronidase.

Franz Heimann.

**A Simple Quantitative Formol-gel Reaction and its Relation to the Euglobulin and Gamma-globulin Content of Serum.** (Een eenvoudige quantitative formolgel-reactie en haar verband met het euglobulinegehalte en gamma-globulinegehalte van het serum.) VERHAGEN, B. A. (1947). *Ned. Tijdschr. Geneesk.*, 4, 3524.

A simple reaction is described for the determination of the  $\gamma$ -globulin content of blood serum. Gel formation of serum occurs after the addition of a calcium-formalin solution when the  $\gamma$ -globulin content is raised. (The values obtained by this method tallied well with those found by electrophoresis.)

Twelve grammes of calcium chloride was dissolved in 100 ml. of water. The specific gravity of the solution should be 1.048, and it should be neutral to bromothymol blue. This solution was mixed in equal parts with a solution obtained by adding to commercial formalin sufficient 4N sodium hydroxide to make the solution neutral to bromo-thymol blue, the formaldehyde content being checked and adjusted to 37 g. per 100 ml. The latter solution remains stable for several months. Mixing was carried out immediately before use.

**Technique.**—Place 10 to 15 tubes ( $8 \times 1.5$  cm.) in a rack—usually 10 suffice. Add to the first tube 1 ml. of serum (24 hours old), to the following tubes add 0.95, 0.9, 0.85 ml., and so on. Add sufficient physiological saline to make the final quantity up to 1 ml. Then add 0.1 ml. of calcium-formalin solution to each tube. Cork with a rubber stopper, shake, and leave at room temperature overnight. A positive result is indicated by complete solidification. Intermediate results are recorded as  $\frac{1}{2}$ ,  $\frac{1}{3}$ , and  $\frac{2}{3}$ . With normal sera no change is observed. Positive results correspond to  $\gamma$ -globulin values as indicated:

Tube No.	$\gamma$ -globulin (g. per 100 ml.)	Tube No.	$\gamma$ -globulin (g. per 100 ml.)
1	1.95	9	3.25
2	2.05	10	3.55
3	2.17	11	3.90
4	2.29	12	4.33
5	2.44	13	4.88
6	2.60	14	5.57
7	2.79	15	6.50
8	3.00		

R. Salm.

**Advantages of a Radiographic Technique with Anterior Cassette in the Study of the Lumbo-sacral Region in the Upright Position. Importance of this Method in the Study of Scoliosis with Pelvic Imbalance.** (Sur les avantages d'une technique "ampoule dorsale—film ventral" pour la radiographie de face de la charnière lombo-sacrée en position de bout. Intérêt de cette méthode pour l'étude des scolioses avec déséquilibre pelvien.) DE SÈZE, S., and COLIEZ, R. (1947). *Rev. Rhum.*, 14, 370.

**Radiological Picture of Subacromial Osteophytosis in a Patient with Pain in the Shoulder.** (Image radiologique d'ostéophytose sous-acromiale chez une malade atteinte d'un syndrome douloureux de l'épaule.) WEISSENBACH, R. J., PERLÈS, L., and LE DINH, T. (1948). *Rev. Rhum.*, 15, 14.

**Rheumatism and Ocular Affection.** (Rhumatisme et affections oculaires.) STROOBANTS, C. (1947). *Acta physiother. rheum. belg.*, 2, 189.

**Experience of Rheumatic Patients who Served in the Armed Forces, 1942–1946.** WILSON, M. G., PAYSON, J. W., and LUBSCHEZ, R. (1948). *Amer. J. publ. Hlth.*, 38, 398.

**Streptococcal Agglutination in Rheumatic Conditions.** (Agglutination streptococcique dans les affections rhumatismales.) COSTE, F., and DELBARRE, F. (1948). *Rev. Rhum.*, 15, 44.

**Ten Years of Treatment of Rheumatism by Radioactive Thermal Waters.** (Considerations sur dix ans de traitement des rhumatismes par les eaux thermales radioactives.) WIRBOTTE, J. (1948). *Rev. Rhum.*, 15, 21.

**Cryotherapy of Subdeltoid Bursitis.** (La cryothérapie de la périarthrite aigue de l'épaule (subdeltoidis bursitis.) MICHOTTE, L. S. (1948). *Rev. Rhum.*, 15, 8.

**Penicillin Therapy of Subacute Infective Arthritis.** (Réflexions sur la penicillinothérapie des arthrites infectieuses subaiguës.) JUSTIN-BESANÇON, L., RUBENS DUVAL, A., and TUBIANA, M. (1947). *Rev. Rhum.*, 14, 356.

**Synthetic Oestrogens in the Treatment of Rheumatism.** (Les oestrogènes de synthèse dans le traitement du rhumatisme.) LAYANI, F., MAY, V., and ATTAL, — (1948). *Bull. Soc. méd. Hôp. Paris*, 64, 199.

**Rheumatism and Gonococcal Phlebitis.** (Reumatismo y flebitis gonococcica.) DE RUGGIERO, F., and BLUVOL, S. (1948). *Rev. argent. Reum.*, 12, 258.



## BOOK REVIEWS

*Archives of Medical Hydrology.* (Journal of the International Society of Medical Hydrology.) Vol. 18, No. 1. April, 1948. John Wright and Sons, Bristol. Simpkin Marshall, London. To be published bi-annually. Price 7s. 6d. or \$2.00 per issue.

The *Archives of Medical Hydrology* had a welcome rebirth in April, when it appeared in a completely new and attractive format, published by John Wright and Sons as a bi-annual journal. There is a foreword by Lord Horder, in which he outlines the history of the International Society of Medical Hydrology, of which he is President. This Society was founded in 1921, and produced the first "Archives" in 1922. The chairman is Dr. Barnes Burt, and the Hon. Secretary Dr. Donald Wilson.

The first post-war number contains papers read at Buxton in 1946, and at Rheinfelden in 1947. The Society is meeting this year at Spa. The articles are contributed by authorities on the Continent and in the U.S.A. as well as in this country, and cover the treatment of peripheral vascular disease, effects of high altitude, and the use of hydrotherapy in poliomyelitis, war injuries, and accidents. There is also a paper by Dr. van Breemen on "Medical Hydrology and the Four Causal Factors in Rheumatic Disease", in which he expresses the view that infection, constitutional anomalies, the skin barrier, and environment are the essential variants. He finishes his paper with the remark: "It is manifest that spa treatment must not be regarded as the last refuge for rheumatic patients, but as a preventative for use in the earliest stages before deformities of the disease are stabilized. This necessitates an effective organization to ensure that all rheumatic patients who need spa treatment can get it, irrespective of their financial status."

We must compliment the International Society of Medical Hydrology on their first post-war number.

G. D. KERSLEY.

*The Rheumatic Diseases.* By G. D. Kersley. Second Edition. 1945. Heinemann: London. Pp. 120; 40 illustrations. Price 15s.

This is an excellent small book in which Dr. Kersley has covered the field of the rheumatic diseases in a delightful and stimulating manner. He has written from the point of view of the physician, but has included chapters on physical medicine which outline in a clear-cut manner the theory and methods of this group of treatments. The chapter on gout is extremely good. The impression is given that the spa method of doing sedimentation rates has superseded the Westergren and Wintrobe techniques but at rheumatism centres outside the spas this is not so.

Wise advice is given on the assessment of radiographs in osteo-arthritis and on the importance of treating the fibrositic element before concluding that the symptoms are due to bony abnormality. One would have liked more stress laid on the value of sling exercises and of hydrotherapy in osteo-arthritis, but these are very small points.

This book should serve two purposes. In little over a hundred pages the practitioner can be brought up to date in his knowledge of the latest views on the theory and treatment of this important group of diseases. The student or physician who wishes to make a more detailed study of the subject might well use this book as his introduction, for Dr. Kersley has included an excellent series of well chosen references for wider reading.

The whole subject is dealt with in a most competent and scholarly manner.

OSWALD SAVAGE.

## HUNTERIAN PROFESSORSHIP

At a meeting of the Council of the Royal College of Surgeons under the chairmanship of Lord Webb-Johnson, P.R.C.S., held on July 8, 1948, Dr. W. S. C. Copeman was elected to an Hunterian Professorship for work on the pathological anatomy of lumbar fibrositis, and more

particularly to the place of oedema and herniation of fat lobules in lumbar and gluteal pain.

Original publications by Dr. Copeman on this work appeared in the *Quarterly Journal of Medicine* for 1944, vol. 18, p. 37, and in the *Archives of Internal Medicine* for 1947, vol. 79, p. 22.